UNIVERSITY OF CRAIOVA

FACULTY OF SCIENCES

DEPARTMENT OF PHYSICS

Laser interaction with matter.

Applications

Thesis Summary

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Craiova 2018

Table of Contents (As they appear in the PhD thesis)

Chapter 1

Introduction

Abstract

The thesis focuses on the laser interaction with matter with application on deposition and characterization of thin films with functional properties. The topic has a high degree of interdisciplinarity involving fundamental areas such as physics, biology and chemistry. Nowadays, the utility of developing nanoscale processing and analysis technologies has led to significant advances in equipment manufacturing. An important factor in their development is played by thin film deposition based on criteria such as low cost, weights and small dimensions.

Two directions are examined: a) deposition of polymeric and biological thin films using Matrix Assisted Pulsed Laser Evaporation (MAPLE) b) deposition of Layered Double Hydroxides (LDH) films using Pulsed Laser Deposition (LPD).

In the first part is described and highlighted the capacity of MAPLE for the deposition of PEG-PVA polymer films which have incorporated into their structure an anti-tumor agent. These aspects are proposed for study due to applications of biodegradable polymers in the medical field and for the anticancerogenic potential of curcumin on cancer cells of osteosarcoma.

Stability and degradability studies, physico-chemical characteristics, functionality of organic molecule demonstrated in *in vitro* biological studies reveal dependence of thin film quality on the solvent used in MAPLE experiments.

In the second part, Pulsed Laser Deposition was chosen as method for obtaining thin films of Layered Double Hydroxides (LDH). The ability of these materials to be tuned in various ways directs attention to diverse applications involving chemistry, environmental sciences and devices based on sensors. X-Ray Diffraction and Fourier Transformed Spectroscopy in Infrared have confirmed the preservation of the crystallinity and chemical structure of bulk deposited as thin film by PLD.

In conclusion, it was demonstrated that laser based thin film deposition technics are appropriate to meet the high requirements and standards imposed by the various application areas.

CHAPTER 1

Introduction

1.1 General overview regarding thin films processing

The multidisciplinary nature of nanoscience, an area at the intersection of the four fundamental sciences - mathematics, physics, chemistry and biology - has generated a high interest among scientists, resulting in fundamental advances in the basic understanding of the various ways of controlling and manipulating matter at the nanoscale, providing nanotechnologies the ability to create technological innovations and affordable products with considerably improved performance.

Predetermination of material properties along with better scientific understanding of the subject allows the development of concrete ideas who leading to technological innovations. These technological innovations do not necessarily require individual atomic control but exploitation of bulk solids properties. In fabrication of these devices an important factor is played by thin film deposition technologies. The importance of thin films is given by the fact that they maintain at least a nanometric dimension.

1.4 Motivation for the current project

Nowadays, advances in science and technology involve the development of the ability to measure, manipulate and organize matter at the nanoscale. These advances will have a major impact on priority areas such as environmental sustainability, health, improvement of living conditions and engineering science. However, this miniaturization should not be done only quantitatively but also qualitatively.

An important area involving these requirements is the production and characterization of thin films. Through thin films we understand a dimensionally reduced material created by the condensation of various atomic, molecular or ionic species of matter, but which preserves the functionality of the initial material. The main challenge is to choose the right method of deposition.

Main proposed objectives: *a) finding and optimizing experimental parameters used in laser-based deposition processes; b) Successful use of Pulsed Laser Deposition (PLD) for the production of high quality thin films of Layered Double Hydroxides (LDH) and LDH incorporating organic molecules and chromophores used for various applications; c) physico-chemical characterization to understand the complex phenomena that occur during the deposition; d) Successful use of Matrix Assisted Pulsed Laser Evaporation for the deposition of*

polymeric-organic hybrid films; e) study of physico-chemical properties and in vitro testing of MAPLE films of great interest for medical applications;

1.5 Configuration of the thesis and short description of each chapter

The thesis is structured in 5 chapters, each completed by the references; at the end is attached the list of publications and presentations of the author at national and international conferences.

The introduction chapter presents the thematic of the paper and the importance of the research field in which it was carried out, the motivation for choosing the themes studied in the thesis and a brief description of each chapter.

Chapter 2 presents the state of the art in pulsed laser deposition techniques as well as aspects related to the investigation methods of the obtained layers. Thus, relevant information about thin film deposition techniques, as Pulsed Laser Deposition (PLD) and Matrix Assisted Pulse Laser Evaporation are explained. The main techniques used for morphological and structural characterizations are also presented: AFM (Atomic Force Microscopy), SEM (Scanning Electron Microscopy), Spectro-Ellipsometry, Ultraviolet-Visible Spectroscopy (UV-VIS), X-Rays Diffraction (XRD), Thermal analysis, and biological characterization methods.

Chapter 3, *In vitro testing of curcumin-based composites coatings as antitumoral systems against osteosarcoma cells*, describes the properties of the materials involved in the study as well as the parameters used in MAPLE deposition of PEG-PVA and PEG-PVA with curcumin. The experimental results obtained on surface morphology (AFM and SEM studies), structural properties (FTIR), degradability and optical properties (SE and UV-VIS studies) are presented and commented.

In chapter 4, *Thin films deposition of the hybrid organo-layered double hydroxides with photofunctional guest molecules within layered double hydroxides (LDH) host matrix* are presented the properties of these materials, their field of applicability as well as the parameters used for their obtaining in the form of powders and subsequently as thin films by Pulsed Laser Deposition.

1.6 References of Chapter 1

[2] Krishna (eds) **HANDBOOK OF THIN-FILM DEPOSITION PROCESSES AND TECHNIQUES Principles, Methods, Equipment and Applications** Second Edition (2001)

[3] S.Krishna (eds) **Handbook of Thin Film Deposition** (2012) Elsevier Science & Technology Books

[4] L.I.Maissel, and R. Clang, (eds.) **Handbook of Thin Film Technology**, McGraw-Hill, New York (1970)

[5] J. L.Vossen, and W. Kern, (eds.) **Thin Film Processes**, Academic Press, New York (1978)

[6] R.F.Bunshah(ed) **Deposition Technologies for Films and Coatings**: Developments and Applications, Noyes Publications, Park Ridge, NJ (1982)

[7] G.Hass,J.B.Ramsey, **Vacuum Deposition of Dielectric and Semiconductor Films by a CO Laser** Appl. Opt. 8, (1969) 1115-1118

[8] H.M.Smith,A.F.Turner - **Vacuum Deposited Thin Films Using a Ruby Laser**, Appl. Opt. 4 (1965) 147-148

[29]A.Pique **The Matrix-Assisted Pulsed Laser Evaporation (MAPLE) process: origins and future directions.** Appl Phys A. 105 (2011) 517-528

[30]A.Pique **Deposition of polymers and biomaterials using the Matrix-Assisted Pulsed Laser Evaporation (MAPLE) process**. Chapter 3 in Pulsed Laser Deposition of Thin Films. Applications-Led Growth of Functional Materials. (R Eason Editor) (2007) 63-84

CHAPTER 2

Theoretical aspects and experimental methods

2.2 Laser techniques for thin film deposition

2.2.1 Pulsed Laser Deposition (PLD)

Introduction

The first attempts to grow thin film using the Pulsed Laser Deposition technique are mentioned in the 1965 experiments [20] when HM Smith and AF Turner, using a ruby laser, ablate material from a target placed in a low-pressure deposition chamber. The poor adherence of the ablated species and the uneven thickness of the film were the main features of these experiments.

In 1987, with the publication of successful YBCO thin film deposition [21], the interest in producing thin films through this technique increased, and this also involved the development of high intensity pulsed laser sources with nano-, pico and femto-seconds time duration.

The principle of Pulsed Laser Deposition (PLD) process

Pulsed Laser Deposition is a thin film growth method based on the interaction of the laser beam with the target material. The high pulse energy with duration of several nanoseconds and in the order of 10^8-10^9 W/cm^2 (corresponding to the Nd: YAG system used in this thesis) is absorbed into the target material, and due to rapid energy conversions involving kinetic energy and heat, results plasma that transfers the ablated particles to a substrate where the film grows.

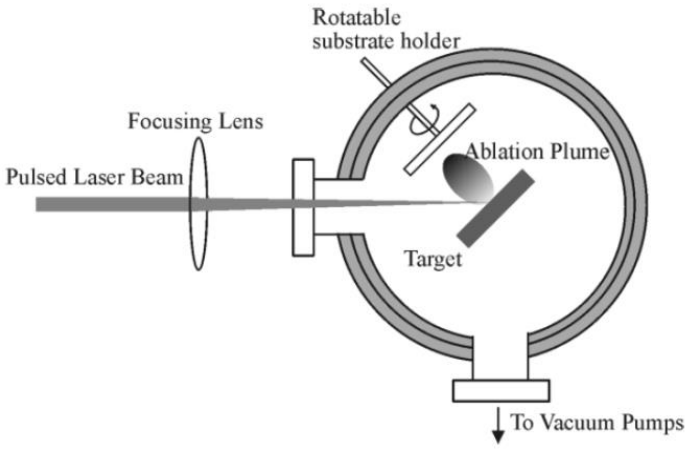

Figure 2.1 Schematic representation of the Pulsed Laser Deposition technique [48]

2.2.2 Matrix-Assisted Pulsed Laser Evaporation (MAPLE)

When using high energy laser pulses, direct application to fragile materials is critical, and therefore the relaxation and excitation processes specific to these techniques can be improved by varying the laser parameters, the material, or both. In MAPLE, a more delicate absorption process is obtained without altering the composition of the material.

In MAPLE [77] [78], a volatile solvent is used as a matrix in which the material of interest is dissolved <5 wt%, resulting in a homogeneous mixture. The next step, after dissolving the solute in the solvent and obtaining the homogeneous solution, is to fast freeze the mixture with liquid nitrogen and obtain a solid target, which will be used later as in PLD experiments [79]. When the incident laser radiation hit the solid target, the energy is absorbed by the solvent and is converted to thermal energy that produces vaporization of the materials from target surfaces [80].

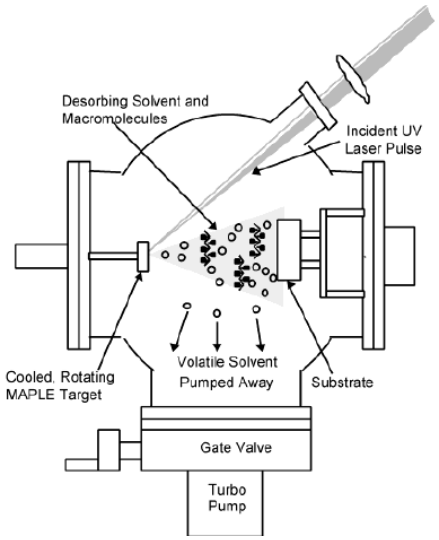

Figure 2.3 Schematic representation of the Matrix-Assisted Pulsed Laser Evaporation technique MAPLE [65]

2.4 References to Chapter 2

[2] J.L.Vossen, and W.Kern, (eds.) **Thin Film Processes** , Academic Press, New York (1978)

[3] R.F.Bunshah (ed) D**eposition Technologies for Films and Coatings: Developments and Applications**, Noyes Publications, Park Ridge, NJ (1982)

[5] K.Seshan **HANDBOOK OF THIN-FILM DEPOSITION PROCESSES AND TECHNIQUES** Principles, Methods, Equipment and Applications Second Edition (2001)

[20] H M.Smith,A.F.Turner **Vacuum Deposited Thin Films Using a Ruby Laser** , Appl. Opt. 4 (1965) 147-148

[21] D.Dijkkamp,T.Venkatesan,X.D.Wu, S.A.Shaheen et al. **Preparation of Y-Ba-Cu oxide superconductor thin-films using pulsed laser evaporation from high T_c bulk material ,** APPLIED PHYSICS LETTERS 51 (1987) 619-621

[22] A.Pique,R.C.R.A.McGill,D.B.Chrisey,et al. **Matrix-assisted pulsed laser evaporation (MAPLE) of polymeric materials: Methodology and mechanistic studies** , ADVANCES IN LASER ABLATION OF MATERIALS Book Series: MATERIALS RESEARCH SOCIETY SYMPOSIUM PROCEEDINGS 526 (1998) 375-383

[29] D.B.Chrisey and G.K.Hubler (editors) **"Pulsed Laser Deposition of Thin Films"**, JohnWiley & Sons Inc., New York, 1994

[30] M.von Allmen,A.Blatter **Laser-Beam Interactions with Materials,** Springer-Verlag,Berlin, 1995. BOOK

[31]D.Bäuerle **Laser Processing and Chemistry** , 3rd ed. (Springer-Verlag, Berlin, Heidelberg, New York 2000)

[32] M. von Allmen, A.Blatter, **Laser-Beam Interactions with Materials** , Springer, Berlin, 2nd ed., 1995

[33] D.Bäuerle, R.Rössler, J.Pedarnig, S.H.Yun, R.Dinu, N.Arnold **Pulsed laser deposition** Appl. Phys. A, 69 (1999) S45-S49

[47] L.V.Zhigilei,B.J.Garrison **Mechanisms of laser ablation from molecular dynamics simulations: dependence on the initial temperature and pulse duration** , Appl. Phys. A, 69 (2009) S75–S80

[48] M.N.R.Ashfold,F.Claeyssens,G.M.Fuge,S.J.Henley **Pulsed laser ablation and deposition of thin films ,** Chem. Soc. Rev. 33 (2004) 23-31

[55] D.B.Chrisey,J.S.Horwitz,R.E.Leuchtner **Excimer laser ablation of a $YBA_2CU_3O_7$-delta target in a vacuum-characterization of the mass and energy of ejected materia** , Thin Solid Films 206 (1991) 111-115

[65] D.B.Chrisey,A.Pique,R.A.McGill,J.S.Horwitz,B.R.Ringeisen,D.M.Bubb,P.K.Wu **Laser deposition of polymer and biomaterial films** , Chem Rev. 103 (2003) 553-576

[69] A.Pique´, R.A.McGill,D.B.Chrisey,D.Leonhardt,T.E.Mslna,B.J.Spargo,J.H.Callahan, R.W.Vachet,R.Chung,M.A.Bucaro **Growth of organic thin films by the matrix assisted pulsed laser evaporation (MAPLE) technique ,** Thin Solid Films 1999, 355-356, 536-541

[70] D.B.Chrisey,A.Pique,R.A.McGill,J.S.Horwitz,B.R.Ringeisen,D.M.Bubb,P.K.Wu . **Laser deposition of polymer and biomaterial films** , Chem Rev. 2003;103:553-576

[71] P.K.Wu,B.R.Ringeisen,J.Callahan,M.Brooks,D.M.Bubb,H.D.Wu,A.Pique,B.Spargo, R.A.McGill,D.B.Chrisey **The deposition, structure, pattern deposition, and activity of biomaterial thin-films by matrix-assisted pulsed-laser evaporation (MAPLE) and MAPLE direct write ,** Thin Solid Films 398 –399 (2001) 607-614

[77] A.Pique **The Matrix-Assisted Pulsed Laser Evaporation (MAPLE) process: origins and future directions ,** Appl Phys A. 105 (2011) 517-528

[78] A.Pique **Deposition of polymers and biomaterials using the Matrix-Assisted Pulsed Laser Evaporation (MAPLE) process.** Chapter 3 in **Pulsed Laser Deposition of Thin Films. Applications-Led Growth of Functional Materials ,** (R Eason Editor). 3 (2007) 63-84

[79] R.Cristescu,D.Mihaiescu,G.Socol,I.Stamatin,I.N.Mihailescu,D.B.Chrisey . **Deposition of biopolymer thin films by matrix assisted pulsed laser evaporation** , Appl Phys A 79 (2004) 1023–1026

[80] A.P.Caricato,S.Capone,M.Epifani,M.Lomascolo,A.Luches,M.Martino, et al.

Nanoparticle thin films deposited by MAPLE for sensor applications , 6985 (2008) 69850H–69850H–13

CHAPTER 3

In vitro testing of curcumin based composites coatings as antitumoral systems against osteosarcoma cells

3.1 Current state of knowledge in the field of anti-cancer coatings

State-of-the-art in cancer research relies on finding new directions in developing effective drugs or bioactive compounds that have minimum cytotoxic effect on healthy cells. This objective has pushed scientific research in the field to pursue complex solutions, which combine existing technologies and materials. In this paper, studies focused on osteosarcoma (OS) cancer.

Osteosarcoma (OS) is defined as a neoplasm that is histologically characterized by the production of osteoid in association with malignant mesenchymal cells. These tumors are generally locally aggressive and tend to produce early systemic metastases. [1]

Curcumin is a hydrophobic polyphenol derived from the rhizome of the Curcuma longa plant. The safety and efficacy of this polyphenol provides a solid basis for being evaluated for clinical applications.

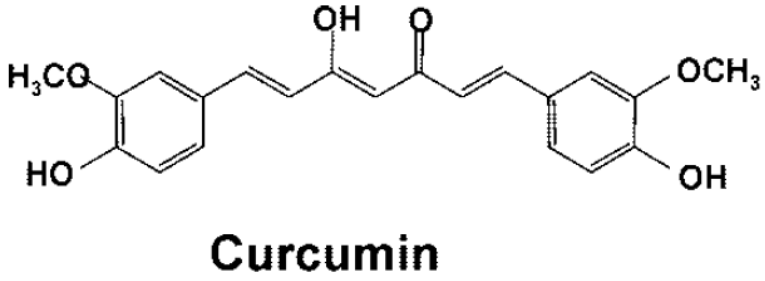

Figure 3.1 Chemical structure of curcumin [16]

Based on preclinical and clinical studies, curcumin showed beneficial effects in several types of cancer, such as: liver [26,27], stomach [28], pancreas [29] and others [30-33]. In most of these studies, curcumin was delivered orally, but its clinical use is limited because of its low bioavailability and hydrophobic nature of the molecule [34], suggesting that the antitumoral activity of oral curcumin may be limited to the gastrointestinal tract [35-38]. Therefore, various novel methods of preparation and delivery were proposed to improve bioavailability of curcumin: polymeric implantable delivery systems [39], micelles [40], nano-delivery systems [41-42] and liposomal encapsulation [43].

3.2 Preparation of samples and description of the experimental method involved in thin films deposition

Poly (ethylene glycol)-Poly(vinyl alcohol) – graft copolymer (PEG-PVA) (Kollicoat® IR)

The polyethylene glycol-polyvinyl alcohol (Polyethyleneglycol) -Poly (vinyl alcohol) graft copolymer (commercially available Kollicoat® IR) is a soluble polymeric solution used for fast release-controlled applications.

PEG-PVA is mainly used as a coating material for dosage forms in the immediate release of the drug, especially for tablets.

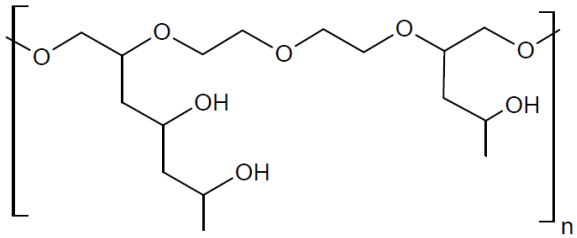

Figure 3.2 Chemical structure of Kollicoat IR (PEG-PVA)

3.2. MAPLE technique

Target	PEG-PVA			PEG-PVA+Curcumin	
Solvent (Matrix)	Chloroform	DMSO	H_20	H_2O+EtOH	Benzene
Concentration of dissolved material	3 %			3%	
Laser wavelength (nm)	266				
Spot size on the target (cm^2)	0.02-0.03				
Laser fluence (J/cm^2)	0.4				
Repetition rate (Hz)	10				
Target-substrate distance (cm)	4				
Number of pulses	27000				
Target rotation (rot/min)	40				
Pressure (mbar)	10^{-4}				

Table 3.1 Parameters used in PEG-PVA and PEG-PVA+Curcumin thin film deposition on glass and Si (001) substrates

3.3 Results and discussions

3.3.1 FTIR analysis of PEG-PVA and PEG-PVA + Curcumin thin films

To evaluate the influence of the solvents on the structural properties of the deposited films, FTIR spectra were acquired for films deposited at 400 mJ/cm^2 laser fluence, with different solvents.

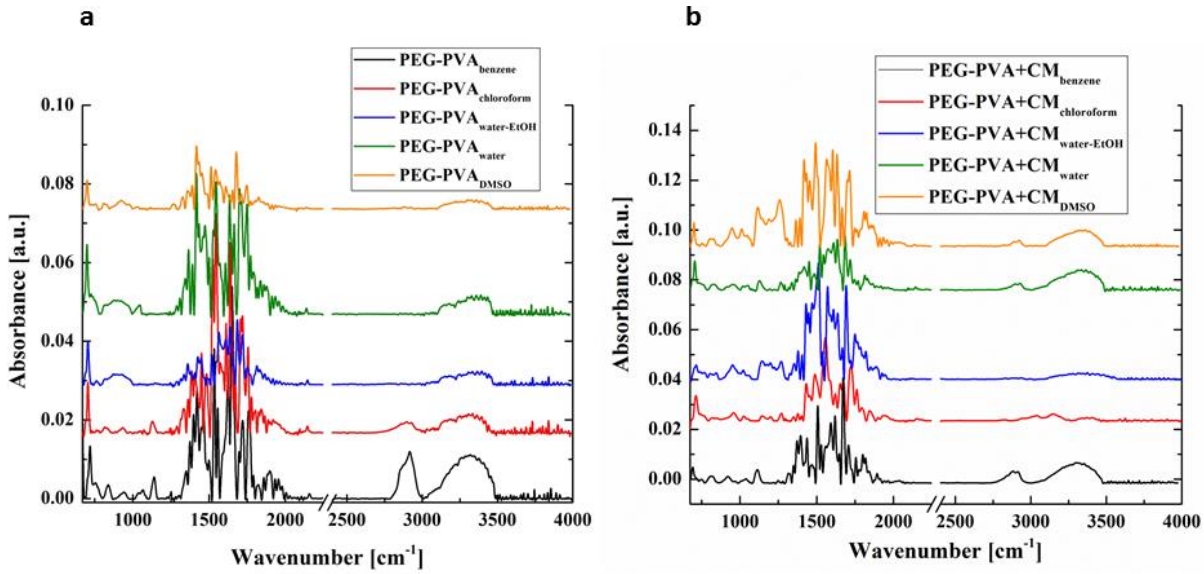

Figure 3.3 Typical infrared bands for the coatings obtained by MAPLE: PEG-PVA (a) and PEG-PVA with embedded curcumin (b)

The embedding of curcumin in the biodegradable copolymer coatings was confirmed by the changes in the spectra, with bands from PEG-PVA and curcumin predominant in all samples obtained with the different solvents.

In our coatings, the curcumin signature is given by the vibration band at 1185 cm^{-1} and 1150 cm^{-1}, assigned to bending of C-O-C in the phenolic part of the curcumin molecule, corresponding to the reported values in the literature. [61].

3.3.3 Surface morphology of PEG-PVA and PEG-PVA + Curcumin thin films

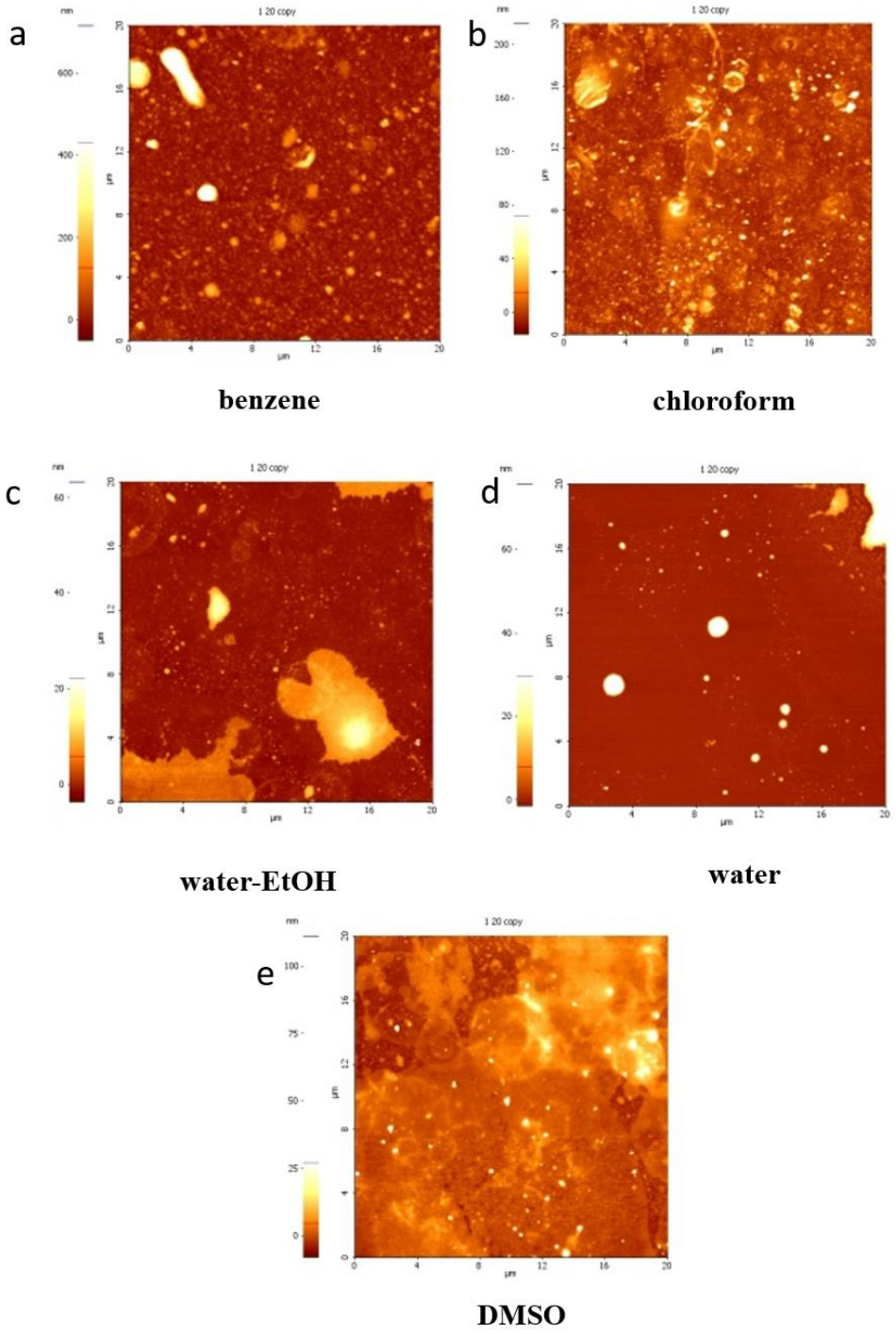

Figure 3.5 AFM images (40 μm x 40 μm) of PEG-PVA coatings obtained by MAPLE using different solvents: benzene (a), chloroform (b), H_2O+EtOH (c), H_2O (d), DMSO(e)

As seen in the AFM images, when using chloroform and DMSO as matrix for the MAPLE depositions, the coatings were characterized by the presence of few nanometer size conglomerates, while in the cases when water and combination of water and ethanol (Fig. 3.5 c, d) were used as solvents, surfaces were characterized by micrometer size droplet-like structures.

An explanation for the non-continuous coatings characterized by the presence of random droplet-like structures is related to the weak absorption of ice water in UV-Vis region, the ablation wavelength used in this work being 266 nm.

Moreover, the curcumin presence within the copolymer coatings led to significant changes in the morphology and covering

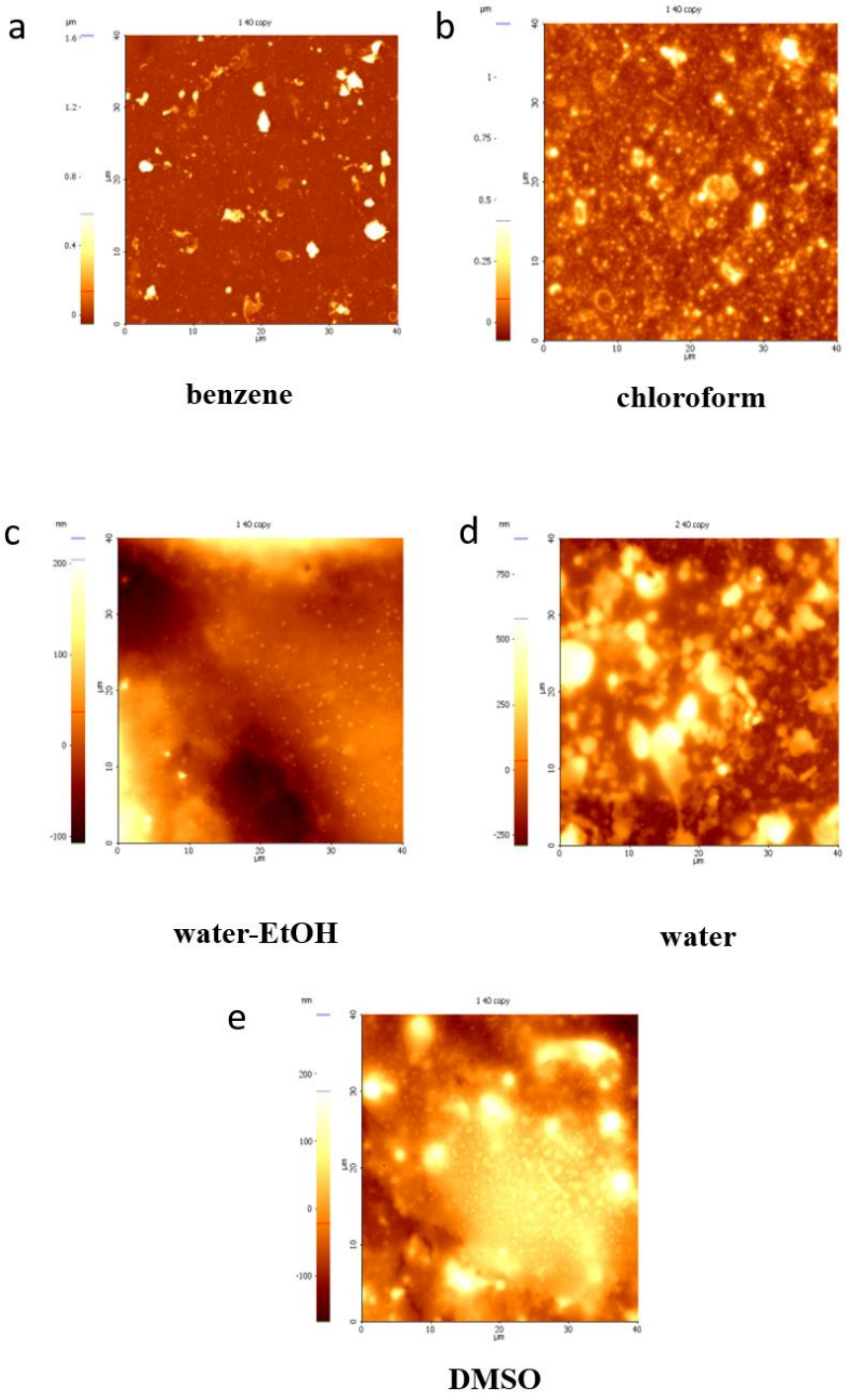

Figure 3.6 AFM images (40 μm x 40 μm) of PEG-PVA with curcumin embedded coatings obtained by MAPLE using different solvents: benzene (a), chloroform (b), H_2O+EtOH (c), H_2O (d), DMSO (e)

3.3.4 Degradation study of PEG-PVA and PEG-PVA + Curcumin thin films

The main problems in terms of controlled drug release are the stability and the degradation behaviors of the films.

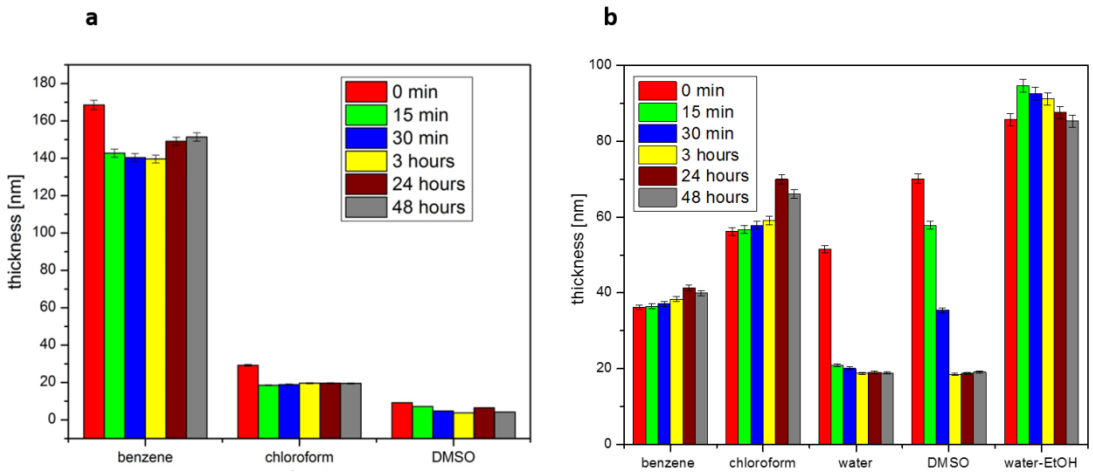

Figure 3.7 Histograms representing the thickness changes after immersing the samples in water: PEG-PVA (a) and PEG-PVA with embedded curcumin (b)

Differences in the thickness of the samples are due to different absorbance of each solvent used for the MAPLE experiments, with the highest absorbing efficiency for benzene and the lowest for water and ethanol.

Axial swelling profiles as a function of time showed that the matrix erosion of PEG-PVA can be split into two stages.

The first stage involved a decrease of 10% in the coatings thickness. The main characteristic of the PEG-PVA$_{benzene}$, PEG-PVA$_{chloroform}$ and PEG-PVA$_{DMSO}$ coatings behavior upon immersion was a rapid decrease of thickness in the first 3 hours, followed by swelling.

In the second stage, an increase in thickness up to 10% in the first 48 hours was noticed. This increase effect could be explained by the presence of both hydrogels-like components, PEG and PVA, in the composition of the thin films obtained by MAPLE (confirmed by FTIR analysis), which preserved similar behavior to bulk hydrogels.

3.3.5 Curcumin release study

Curcumin was released by degradation of thin films, regardless of drug solubility in the dissolution medium, and its release into water was confirmed by UV-Vis measurements (Figure 3.9 a-e). The release of curcumin from PVA-PEG copolymers largely depended on the solvents used (Fig. 3.9 f).

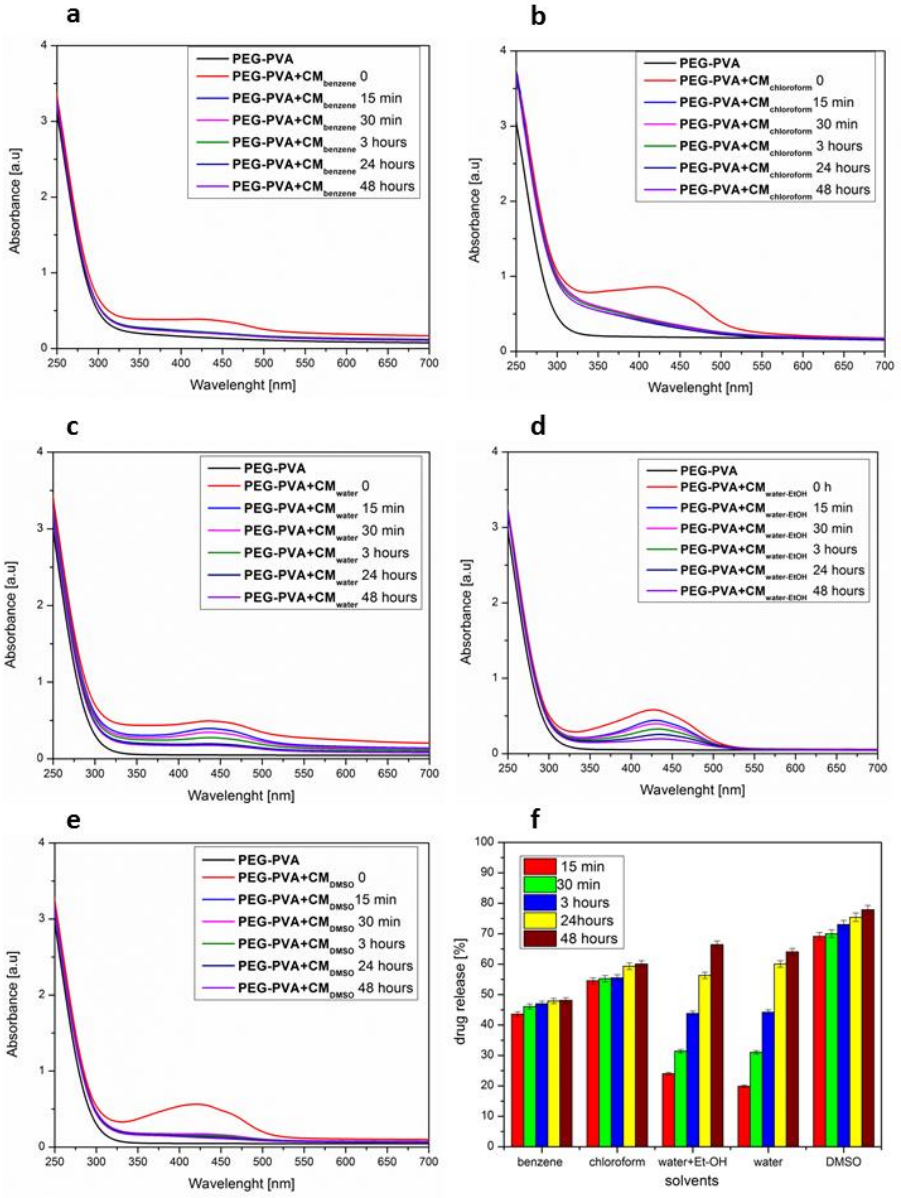

Figure 3.9 Release of curcumin from PEG-PVA copolymers obtained by MAPLE for different solvents: benzene (a), chloroform (b), H_2O+EtOH (c), H_2O (d), DMSO (e); drug release percentage vs. time (f)

According to our expectations, faster degradation resulted in accelerated drug release, behavior confirmed for PEG-PVA+CM$_{water}$, PEG-PVA+CM$_{water-EtOH}$ and PEG-PVA+CM$_{DMSO}$ coatings.

3.3.6 In vitro cellular response of PEG-PVA and PEG-PVA + Curcumin thin films

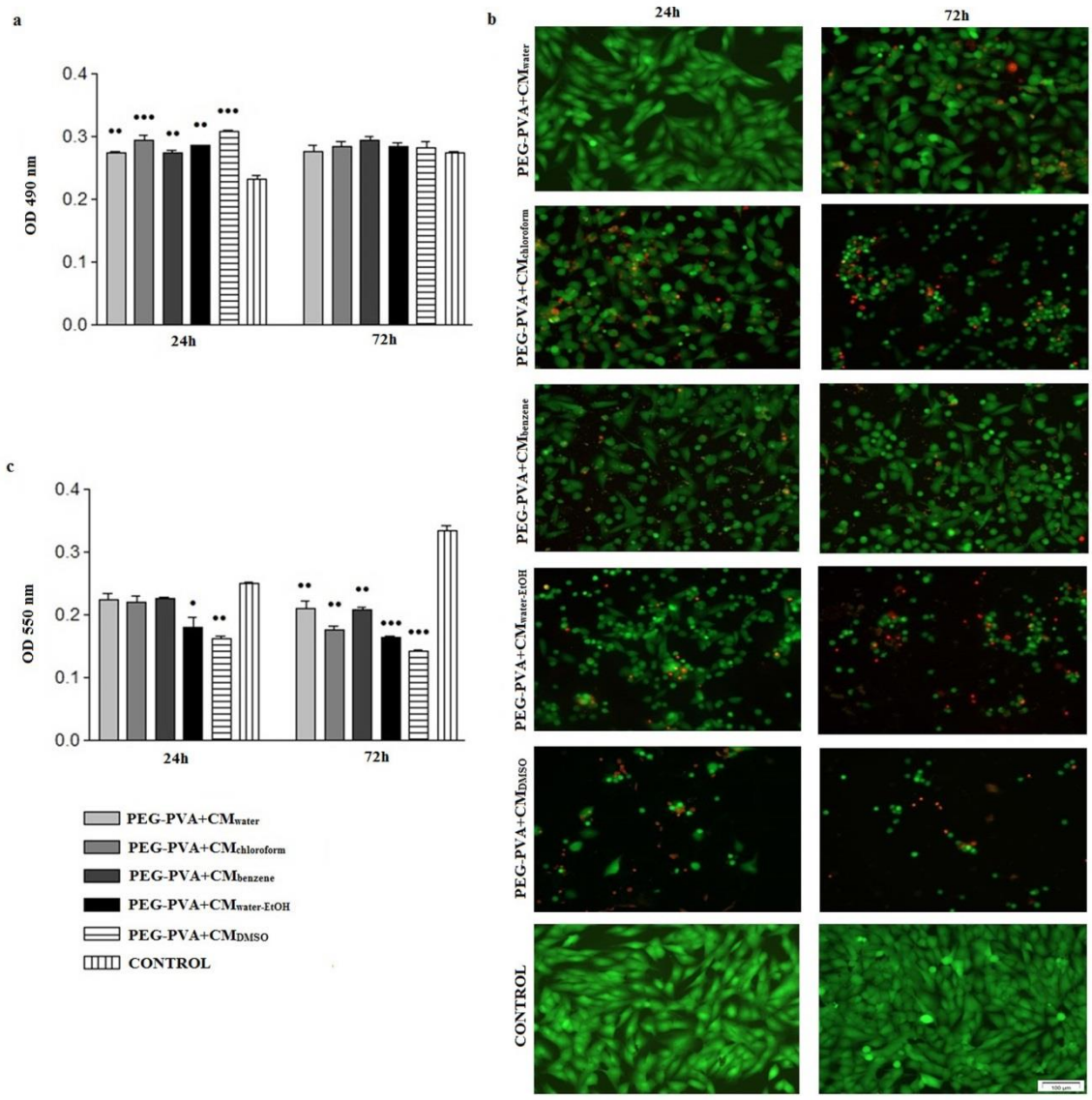

Figure 3.11 Cytotoxicity/Viability/Proliferation of MG-63 osteosarcoma cells grown on PEG-PVA-curcumin-based thin films for 24 and 72 h. (a) LDH assay (n = 3, mean ± standard deviation); (b) Live/Dead assay (live cells are green labeled and dead cells are red labeled); (c) MTT assay (n = 3, mean ± standard deviation). $p<0.05$; $p<0.01$; $p<0.001$ (versus control substrate).

As already noticed, curcumin can inhibit the growth of a variety of tumor cells and induce apoptosis, so as to exert it's *in vivo* and *in vitro* anti-tumor activity [74-76]. *In vitro* cytocompatibility studies performed on the osteosarcoma cell line MG-63 aimed at evaluating cytotoxic effects and cell survival and proliferation supporting activities of PEG-PVA with curcumin embedded thin films. For all experiments, the glass substrates were used as a control sample.

Likewise, the MTT proliferation assay (Fig 3.11 c) revealed decreased cell viability of MG-63 osteoblasts grown on PEG-PVA+$CM_{H2O-EtOH}$ ($P<0.05$) and PEG-PVA+CM_{DMSO} ($P<0.01$), as compared to the control substrate at 24 h post-seeding.

These data are consistent with the results reported by Chang et al. [77] showing that MG-63 osteosarcoma cells were more sensitive to curcumin-induced cytotoxicity than healthy human osteoblasts.

3.4 Conclusions of Chapter 3

In this paper we evidenced the capability of the MAPLE technique for the deposition of curcumin based composite coatings as anti-tumor drug delivery systems. It was demonstrated that solvent represents a key parameter in tailoring the composite coatings morphology, thickness and roughness, with impact on coating stability and on its degradation when exposed to aqueous media.

Rapid degradation characterized by the exponential decrease in thickness was observed for PEG-PVA+CM_{water} and PEG-PVA+CM_{DMSO} thin films, while PEG-PVA+$CM_{water-ethanol}$ and PEG-PVA+$CM_{benzene}$ had a slower degradation rate. The chemical structure and functionality of the curcumin molecules within the biodegradable PEG-PVA copolymer was confirmed by FTIR analysis and bioassays.

Biological evaluation of the developed PEG-PVA+curcumin-based thin films in terms of cell viability and proliferation of MG-63 osteosarcoma cells demonstrated their cytotoxic and anti-proliferative potentials. Noteworthy, the most active is the PEG-PVA+CM_{DMSO} thin film.

The data demonstrate that MAPLE can be employed for the growth of high quality polymeric thin films with embedded anti-tumor compound, which show promising potential for biomedical applications.

3.5 References to Chapter 3

[1] A.K.Raymond,N.Jaffe **Osteosarcoma multidisciplinary approach to the management from the pathologist's perspective** , Cancer Treat Res 152 (2009) 63–84.

[26] G.Kaur, N.Tirkey,S.Bharrhan,V.Chanana,et al. **Inhibition of oxidative stress and cytokine activity by curcumin in amelioration of endotoxin-induced experimental hepatoxicity in rodents** , Clin. Exp. Immunol. 145 (2006) 313–321

[27] R.K.Kempaiah,K.Srinivasan **Influence of dietary curcumin,capsaicin and garlic on the antioxidant status of red blood cells and the liver in high-fat-fed rats** , Ann. Nutr. Metab. . 48 (2004) 314–320

[28] R.Thapliyal,G.B.Maru **Inhibition of cytochrome P450 lisozymes by curcumins in vitro and in vivo** , Food Chem. Toxicol. 39 (2001) 541-547.

[29] A.Masamune,N.Suzuki,K.Kikuta,M.Satoh, et al. **Curcumin blocks activation of pancreatic stellate cells** , J. Cell. Biochem. 97 (2006) 1080-1093

[30] M.Lopez-Lazaro **Anticancer and carcinogenic properties of curcumin: Considerations for its clinical development as a cancer chemopreventive and chemotherapeutic agent** , Mol Nutr Food Res 52 (2008) S103-S127

[31] P.Basnet,N.Skalko-Basnet **Curcumin: An Anti-Inflammatory Molecule from a Curry Spice on the Path to Cancer Treatment** , MOLECULES 16 (2011) 4567-4598

[32] J.Ravindran,S.Prasad, and B.B.Aggarwal **Curcumin and Cancer Cells: How Many Ways Can Curry Kill Tumor Cells Selectively**, AAAPS JOURNAL. 11 (2009) 495–510

[33] A.Goel, A.B.Kunnumakkara,B.B.Aggarwal **Curcumin as ''Curecumin'': From kitchen to clinic** , Biochem. Pharmacol. 75 (2008) 787-809

[34] B.B.Aggarwal, C.Sundaram,N.Malani et al. **Curcumin: The Indian solid gold MOLECULAR TARGETS AND THERAPEUTIC USES OF CURCUMIN IN HEALTH AND DISEASE Book Series: ADVANCES IN EXPERIMENTAL MEDICINE AND BIOLOGY** Adv. Exp. Med. Biol. 59 5 (2007) 1+

[35] B.B.Aggarwal,A.Kumar,A.C.Bharti **Anticancer potential of curcumin: Preclinical and clinical studies** , Anticancer Res. 23 (2003) 363-398

[36] R.K.Maheshwari, A.K.Singh, J.Gaddipati et al. **Multiple biological activities of curcumin: A short review**, Life Sci. 78 (2006) 2081-2087

[37] P.Anand, A.B.Kunnumakkara,R.A.Newman , et al. **Bioavailability of Curcumin: Problems and Promises** , Mol. Pharm. 4 (2007) 807-818

[38] A.Duvoix, R.Blasius,S.Delhalle , et al. **Chemopreventive and therapeutic efects of curcumin**, Cancer Lett. 223 (2005) 181-190

[39] S.S.Bansal, M.V.Vadhanam,R.C.Gupta **Development and in vitro-in vivo evaluation of polymeric implants for continuous systemic delivery of curcumin** , Pharm. Res. 28 (2011) 1121-1130

[40] Z.Ma, A.Haddadi,O.Molavi,A.Lavasanifar,R.Lai,J.Samuel **Micelles of poly(ethylene oxide)-b-poly(ε-caprolactone) as vehicles for the solubilization, stabilization, and controlled delivery of curcumin** , J Biomed Mater Res A 86A (2008) 300-310

[41] R.K.Basniwal,H.S.Buttar,V.K.Jain,N.Jain **Curcumin nanoparticles: preparation, characterization, and antimicrobial study** , J. Agric. Food Chem. 59 (2011) 2056-2061

[42] W.Wu,J.Shen,P.Banerjee , et al. **Water-dispersible multifunctional hybrid nanogels for combined curcumin and photothermal therapy** , BIOMATERIALS 32 (2011) 598-609

[43] M. di Cagno,J.Styskala,J.Hlaváč,M.Brandl,A.Bauer-Brandl,N.Skalko-Basnet, **Liposomal solubilization of new 3-hydroxy-quinolinone derivatives with promising anti-cancer activity: A screening method to identify maximum incorporation capacity**, J Liposome Res 21 (2011) 272-278

[54] A.Pique, R.C.R.A.McGill, D.B.Chrisey , et al. **Matrix-assisted pulsed laser evaporation (MAPLE) of polymeric materials: Methodology and mechanistic studies** , ADVANCES IN LASER ABLATION OF MATERIALS Book Series: MATERIALS RESEARCH SOCIETY SYMPOSIUM PROCEEDINGS 526 (1998) 375-383

[55] V.Dinca, P.E.Florian, L.E.Sima et al, **MAPLE-based method to obtain biodegradable hybrid polymeric thin films with embedded antitumoral agents** , Biomed Microdevices 16 (2014) 11-21

[56] L.Rusen,P.Neacsu,A.Cimpean,I.Valentin,S.Brajnicov,L.N.Dumitrescu,J.Banita,V. Dinca,M.Dinescu **In vitro evaluation of poly(ethylene glycol)-block-poly(É›-caprolactone)**

methyl ether copolymer coating effects on cells adhesion and proliferation , Appl Surf Sci, 374 (2016) 23-30

[57] L.Rusen,V.Dinca,B.Mitu,C.Mustaciosu,M.Dinescu **Temperature responsive functional polymeric thin films obtained by Matrix Assisted Pulsed Laser Evaporation for cells attachment-detachment study** , Appl Surf Sci. 302 (2014) 134-140

[58] A.L.Mercado,C.E.Allmond,J.G.Hoekstra , et al. **Pulsed laser deposition vs. matrix assisted pulsed laser evaporation for growth of biodegradable polymer thin films** , Appl Phys A Mater Sci Process 81 (2005) 591-599

[59] A.Purice,J.Schou, M.Dinescu **Particle emission from polymer doped water ice matrices induced by non-linear absorption of laser light at 1064 nm** , Chem. Phys. Lett. 427 (2006) 251–254

[60]. BASF AG, Technical Information Kollicoat® IR, Homepage BASF AG, http://www.pharmasolutions.basf.de/pdf/Statements/Technical%20Informations/Pharma%20Solutions/EMP%20030724e_Kollicoat%20IR.pdf.

[61] M.S.Ali, V.Pandit, M.Jain,K.L.Dhar **Mucoadhesive microparticulate drug delivery system of curcumin against Helicobacter pylori infection: Design, development and optimization** , J Adv Pharm Technol Res. 5 (2014) 48-56

[64] A.Pique,R.C.R.A. McGill, D.B.Chrisey, et al. **Matrix-assisted pulsed laser evaporation (MAPLE) of polymeric materials: Methodology and mechanistic studies** , ADVANCES IN LASER ABLATION OF MATERIALS Book Series: MATERIALS RESEARCH SOCIETY SYMPOSIUM PROCEEDINGS 526 (1998) 375-383

[74] M.Bernabe-Pineda, M.T. Ramirez-Silva,M.Romero-Romo , et al. **Determination of acidity constants of curcumin in aqueous solution and apparent rate constant of its decomposition** , Spectrochim Acta A Mol Biomol Spectrosc 60 (2004) 1091-1097

[75] K.I.Priyadarsini **The Chemistry of Curcumin: From Extraction to Therapeutic Agent** , MOLECULES 19 (2014) 20091-20112

[76] G.Mudduluru,J.N.George-William,S.Muppala,I.A.Asangani,R.Kumarswamy,L.D. Nelson,H.Allgayer **Curcumin regulates miR-21 expression and inhibits invasion and metastasis in colorectal cancer** , Biosci Rep 31 (2011) 185- 197

[77] G.H. Zhu,H.P.Dai,Q.Shen,O.Ji,Q.Zhang,Y.L.Zhai **Curcumin induces apoptosis and suppresses invasion through MAPK and MMP signaling in human monocytic leukemia SHI-1 cells** , Pharm Biol 54 (2015) 1303-1311

Chapter 4

Deposition of thin films of layered double hydroxides containing photofunctional guest molecules

4.1 Introduction

Layered Double Hydroxides (LDH), known as Hydrotalcite (HT) compounds, are a class of materials with lamellar structure in which the positive charge of the metallic hydroxide brucite layers is compensated by the replaceable anion from interlayer region which can be inorganic, metallo-organic anions, molecules containing ionizable acidic groups or organic anions [1].

The general chemical formula is as follows: $[M^{2+}_{1-x}M^{3+}_{x}(OH)_2]^{x+}(A^{n-}_{x/n}) \cdot mH2O$, where M^{2+} and $M^{3+}$are divalent metal cations (Mg^{2+}, Ni^{2+}, Zn^{2+} or Co^{2+}) respectively trivalent metal cations (Al^{3+}, Cr^{3+}, Fe^{3+}, or Ga^{3+}) [2] [3], A^{n-} represents an anion with charge n such as CO_3^{2-}, Cl^-, NO_3^- or an interlamellar organic anion, and x represents $M^{3+}/(M^{2+} + M^{3+})$ ranging between 0.2 and 0.33 and determines the charge density of the layer and the anion exchange capacity.

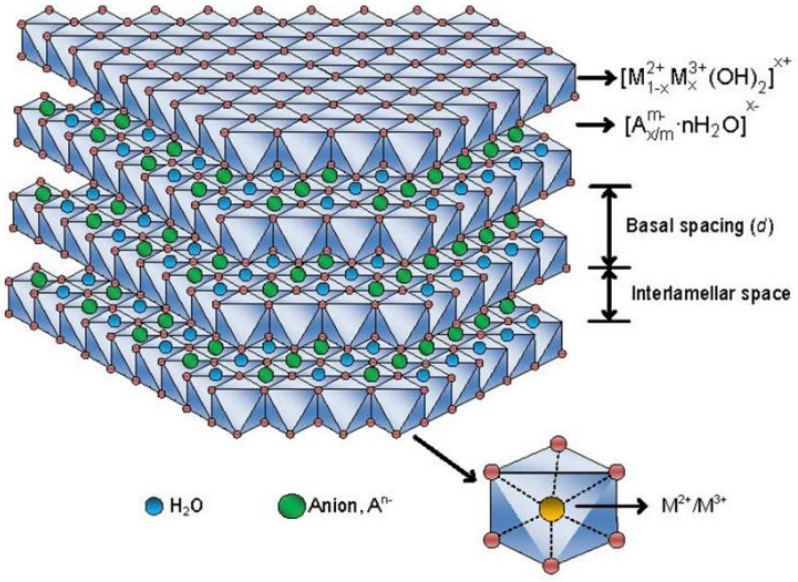

Figure 4.1 Schematic representation of the LDH structure

Structural anisotropy and high anion exchange capacity have led to the rapid expansion of research in LDH materials field, nowadays being extensively used in areas such as catalysis, fluorescent and optical materials [4-7], medicine and pharmaceutics. [1]

The main scientific objective of the thesis was the obtaining of hybrid powders made of organic chromophores - the "guest" coumarin 343 intercalated in the Mg-Al LDH "host" matrix

and subsequently the fabrication, by laser techniques, of functional thin films used in applications as detection sensors.

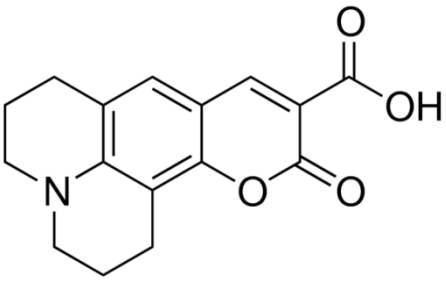

Figure 4.2 Chemical structure of Coumarin 343

Main property of the coumarin compounds is fluorescence displayed in UV light, this high photo-sensitivity being exploited in applications such as dye lasers [15], biological sensors [16] and anionic exchange [17].

Formation of dye aggregates in the host matrix is an important problem in their use, hence to eliminate the aggregation of the chromophores, a second anion used as a surfactant is pre-intercalated in the hydrotalcite matrix. By the introduction of this surfactant Dodecyl Sulfate (DS), the spacing between the layers increases and thus the large molecules of the dye anions can be intercalated between the layers of the Layered Double Hydroxide.

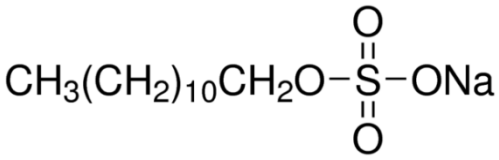

Figure 4.3 Chemical structure of Dodecyl Sulfate -DS

In order to determine the optimal parameters used in thin film deposition experiments, their properties will be compared with those of the starting material.

4.2 Sample preparation and experimental processing of materials

4.2.1 Preparation of Layered Double-Hydroxide powders used as reference samples. Preparation of MgxAl LDH powder (x = 2.5)

4.2.2 Preparation of Mg/Al- LDH powders Dodecyl Sulfate (DS)-modified

4.2.2.1 Preparation of Mg/Al- LDH powders Dodecyl Sulfate (DS)-modified by co-precipitation

The Mg_xAl LDH powder in the molar ratio Mg / Al = 2.5 and LDH with intercalated Dodecyl Sulfate Surfactant (DS SDS=$NaCl_{12}H_{23}S$) was obtained following a protocol used by Wei et al. [35] for intercalating L-tyrosine in NiAl , MgAl and ZnAl-LDH and improved by Du et al. [36] to produce NiAl-LDH with intercalated Dodecyl Sulfate anions. Two methods will be involved in making these powders: coprecipitation and reconstruction.

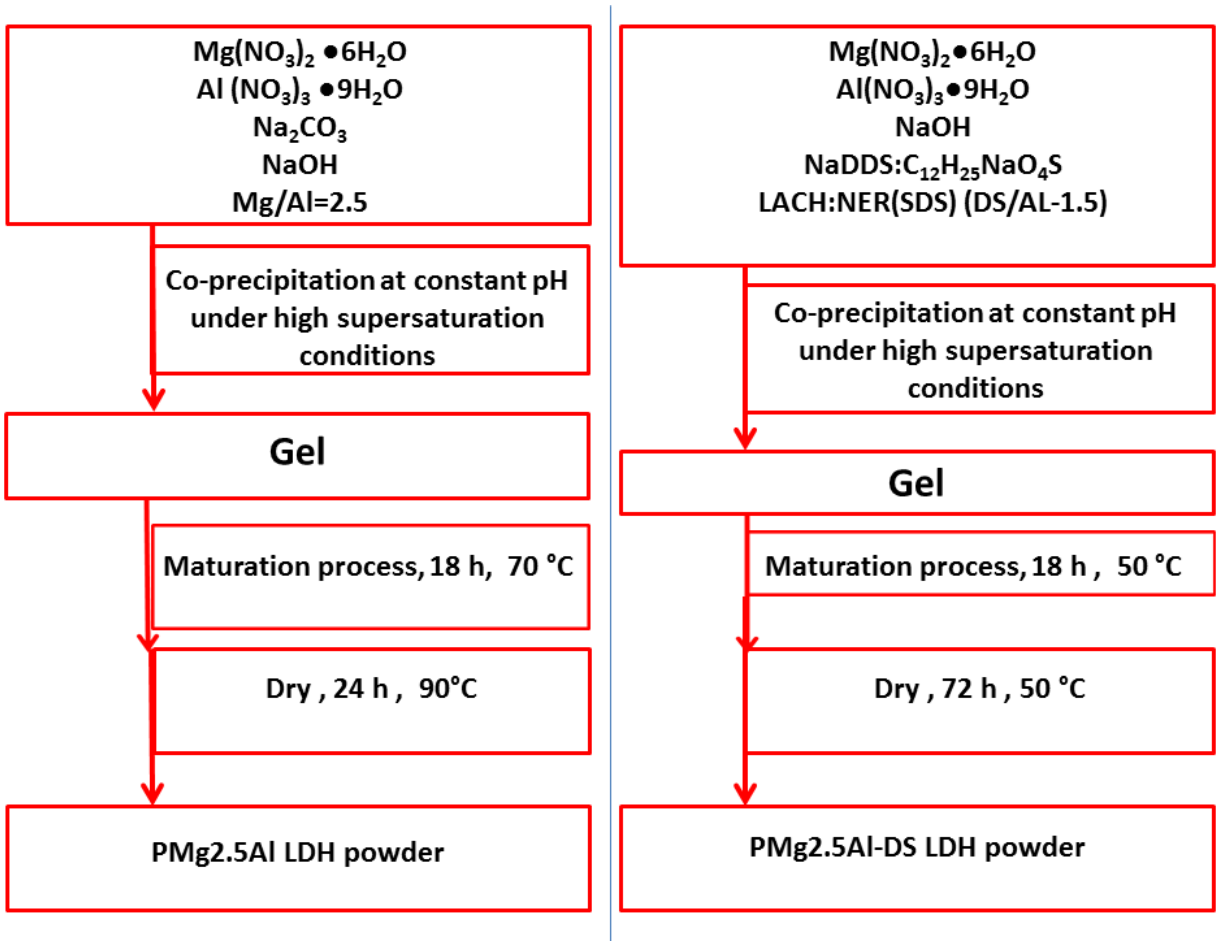

Figure 4.4 Schematic representation of the route followed for obtaining PMg2.5Al-LDH and PMg2.5Al-DS LDH powder

4.2.2.3 Preparation of Mg/Al- LDH powders with intercalated coumarin

It has been preferred to prepare Mg / Al-LDH powders by coprecipitation and for coumarin intercalation between layers of LDH reconstitution from the coumarin aqueous solution in water was chose as method

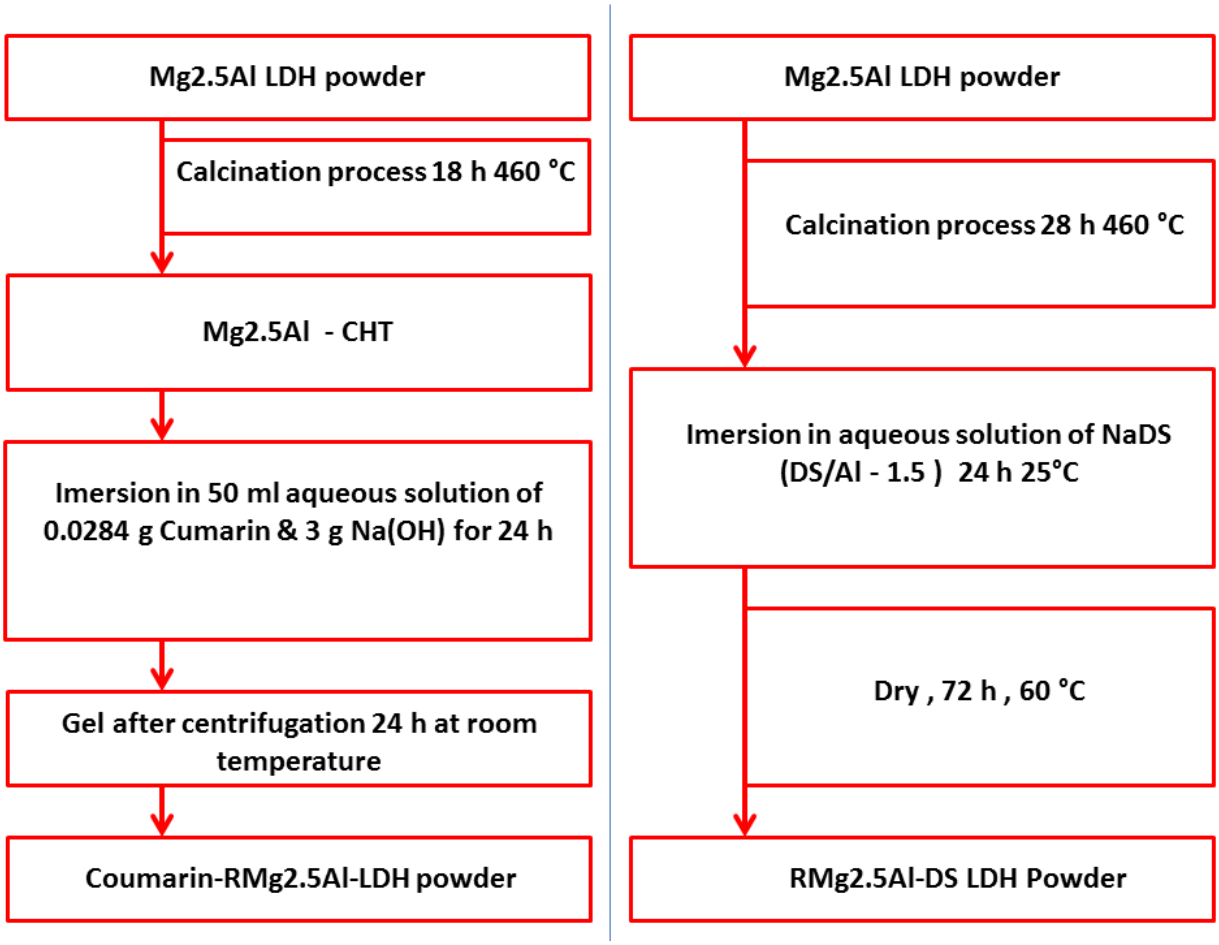

Figure 4.5 Schematic representation of the route followed for obtaining R-coumarin-Mg2.5Al-LDH and R -Mg2.5Al-LDH powder

4.3 Thin films deposition of the hybrid organo-layered double hydroxides with guest molecules within LDH host matrix using Pulsed Laser Deposition

4.3.1 Thin films deposition of Mg/Al- LDH Dodecyl Sulfate (DS)-modified

The deposition experiments by PLD of LDH and LDH+DS thin films are synthesized in Table 4.1

Target	Mg2.5Al, PMg2.5Al-DS , RMg2.5Al-DS		
Laser type	Nd:YAG laser		
Substrates	Glass , Si (001)		
Laser wavelength (nm)	266	532	1064
Spot size on the target (cm^2)	0.01		
Laser fluence (J/cm^2)	2		
Repetition rate (Hz)	10		
Target-substrate distance (cm)	4		
Number of pulses	20000		
Target rotation (rot/min)	40		
Pressure (mbar)	$\sim 10^{-3} - 10^{-4}$ mbar		

Table 4.1 Parameters used in Mg2.5Al, PMg2.5Al-DS and RMg2.5Al-DS thin film deposition on glass and Si (001) substrates

4.3.2 Thin films deposition of Mg/Al- LDH Coumarin-modified

The targets of Mg2.5Al&coumarin LDH used in PLD experiments were obtained by pressing the powders without heat treatment.

The deposition experiments by PLD of LDH and LDH+Coumarin thin films are synthesized in Table 4.2

Target	Mg2.5Al-LDH and RMg2.5Al &coumarin-LDH	
Laser type	Nd:YAG laser	
Substrates	Glass,Si (001)	
Laser wavelength (nm)	532	1064
Spot size on the target (cm^2)	0.01	
Laser fluence (J/cm^2)	2	
Repetition rate (Hz)	10	
Target-substrate distance (cm)	4	
Number of pulses	20000	
Target rotation (rot/min)	40	
Pressure (mbar)	$\sim 10^{-3} - 10^{-4}$ mbar	

Table 4.2 Parameters used in Mg2.5Al-LDH and RMg2.5Al &coumarin-LDH thin film deposition on glass and Si (001) substrates

4.4 Results and discussions

4.4.1 X-ray diffraction(XRD)

4.4.1.1 XRD Characterization of PMg2.5Al, PMg2.5Al-DS and RMg2.5Al-DS powder

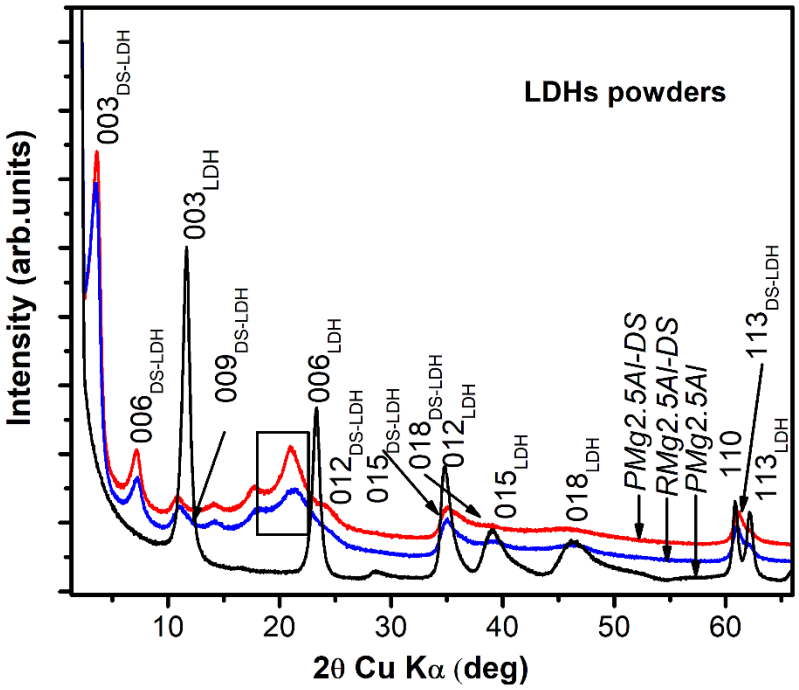

Figure 4.6 Representative XRD patterns for the powders PMg2.5Al, PMg2.5Al-DS and RMg2.5Al-DS

The XRD patterns of PMg2.5Al, PMg2.5Al-DS and RMg2.5Al-DS powders are presented in Fig 4.6. The spectra were recorded using the Bragg-Brentano configuration and the XRD patterns confirm the DS interlayer intercalation. The reference PMg2.5Al sample, exhibits a XRD pattern characteristic of a LDH material structure with a rhombohedral symmetry (JCPDS file 54-1029) and was Miller indexed in a hexagonal lattice. For the DS-modified samples a shift of the (003), (006), and (009) basal spacing reflections to lower 2θ values occurred along with the preservation of the position of the brucite sheet (110) reflection.

The calculated lattice parameters are obtained by a =2 x d110 and c = (3/2) x (d003+2d006), respectively. The interlayer free spacing (IS) was calculated by subtracting the Miyata's reported brucite sheet thickness of 0.48 nm from the c/3, resulting values from Table 4.3 The increase in the interlayer distance was estimated to be approximately 2.14 nm and 2.01 nm, respectively, indicating that the DS is present in the interlayer space.

The Scherrer mean crystallites sizes were evaluated separately from the broadness of the (003) reflection, related to the c-axis along which the layers are stacked, and from the (110) reflection, related exclusively to the brucite-like sheets structure.

Powder samples	Phase comp.	Structural data					
		a / nm	c / nm	IS /nm	D_{001} / nm	D_{110} / nm	Tilt angle
PMg2.5Al	LDH phase	0.305	2.288	0.28	16	37	-
PMg2.5Al-DS	DS-LDH phase	0.304	7.877	2.14	8	37	90
RMg2.5Al-DS	Dominant DS-LDH	0.304	7.462	2.01	11	13	75

Table 4.3 The phase composition and the structural data of LDH and DS-LDH powders

The tilt angle of the intercalated anion was estimated using the formula proposed by Meyn et al [46].

The tilt angle higher for the RMg2.5Al-DS powder suggests a stronger electrostatic force between the layers and the interlayer anions in comparison with the PMg2.5Al-DS, hence a higher thermal stability.

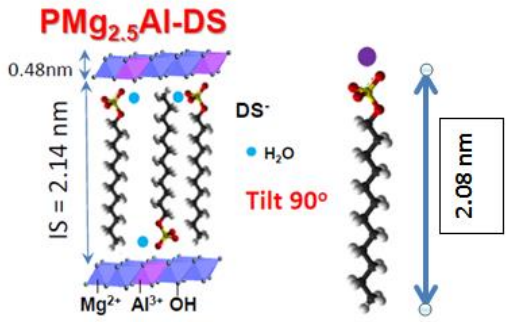

Figure 4.7 DS molecule representation and their interlayer intercalation

4.4.1.2 XRD Characterization of Mg2.5Al-LDH, RMg2.5Al and RMg2.5Al&coumarin powder

The analysis of XRD patterns (Fig 4.8) of Mg2.5Al-LDH, of reconstructed RMg2.5Al LDH and of RMg2.5Al&coumarin LDH samples exhibits sharp and align peaks characteristic at low angles, corresponding to the basal 00l reflection of the crystalline Layered Double Hydroxide structure. Weak intensity peaks are also visible at higher angles. No other peaks assigned to coumarin are present.

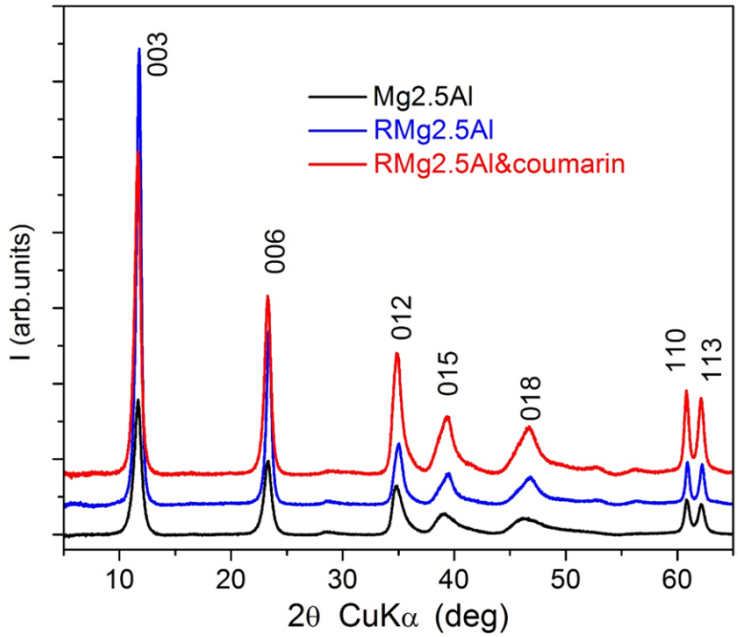

Figure 4.8 Representative XRD patterns for the powders Mg2.5Al-LDH, RMg2.5Al and RMg2.5Al&coumarin

The calculated lattice parameters are obtained by a =2 x d110 and c = (3/2) x (d003+2d006), respectively. The Scherrer mean crystallites sizes were evaluated separately from the broadness of the (003) reflection, related to the c-axis along which the layers are stacked, and from the (110) reflection, and the values resulting are depicted in Table 4.4

Powders	Lattice parameters		I_{003}/I_{110}	Crystallite size	
	a (Å)	c(Å)		D_{003} (nm)	D_{110}(nm)
Mg2.5Al-LDH	3.0454	22.7810	3.316	9	20
Coumarine Mg2.5Al-LDH	3.0456	22.8433	3.840	13	21

Table 4.4 The calculated lattice parameters obtained from XRD patterns of Mg2.5Al-LDH&Coumarine and Mg2.5Al-LDH

4.4.2 Thermogravimetric analysis and differential scanning calorimetry

4.4.2.1 Thermogravimetric analysis and Differential Scanning Calorimetry (TG and DSC) of PMg2.5Al, PMg2.5Al-DS and RMg2.5Al-DS powders

The effective intercalation of surfactant and thermal stability have been proven by thermogravimetric analysis (TGA) and differential scanning calorimetry (DSC) for all of self-synthesized powders (Fig 4.9 and Table 4.5).

Samples	Loss of adsorbed water		Release of interlayer water		Layer Dexydroxylation & loss of interlayer carbonate		Removal of interlayer residuals species		Total weight loss / %
Pristine - LDH	Weight / %	Temperature domain / ^{o}C [Tmax]	Weight / %	Temperature domain / ^{o}C [Tmax]	Weight / %	Temperature domain / ^{o}C [Tmax]	Weight / %	Temperature domain / ^{o}C [Tmax]	
PMg2.5Al	2.5	Rt-135 [107]	13.4	135-300 [250]	27.2	300-800 [440]	0	800-1000	43.1
DS-modified - LDH	Loss of adsorbed and interlayer water		Release of interlayer water &organic portion of DS		Layer Dexydroxylation & loss of anionic sulfate		Removal of interlayer residuals species		
	Weight / %	Temperature domain / ^{o}C	Weight / %	Temperature domain / ^{o}C[Tmax]	Weight / %	Temperature domain / ^{o}C [Tmax	Weight / %	Temperature domain / ^{o}C [Tmax	
PMg2.5Al -DS	8.6	Rt-140 [120]	35.0	140-300 [250]	10.9	300-570 [460]	2.0	570-1000 [670]	56.5
RMg2.5Al -DS	8.2	Rt-140 [125]	30.8	140-300 [270]	11.8	300-555 [460]	2.9	555-1000 [700]	53.7

Table 4.5 Thermal analysis data of the DS-modified LDHs and of the pristine LDH powders

Comparison of TGA curves of PMg2.5Al, PMg2.5Al-DS and RMg2.5Al-DS confirm the intercalation of DS between the layers.

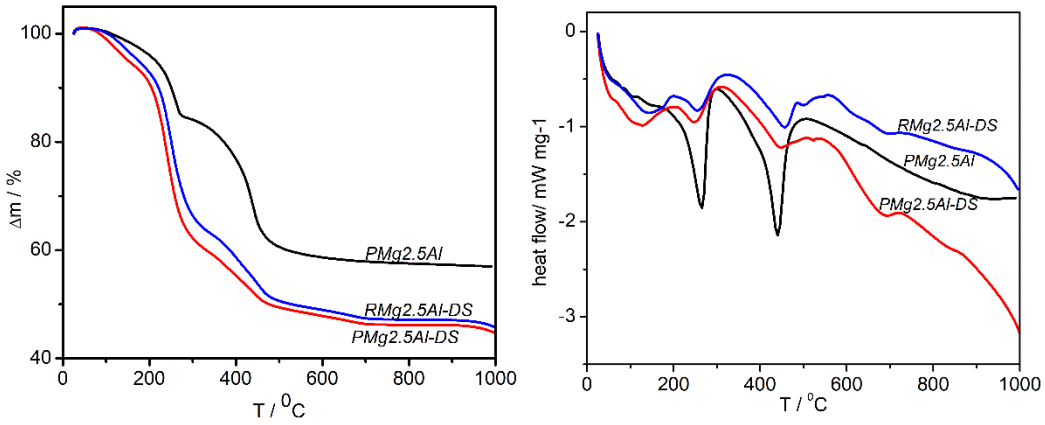

Figure 4.9 TGA and DSC diagrams of the as prepared DS modified LDHs and pristine LDH powders

4.4.2.2 Thermogravimetric analysis and Differential Scanning Calorimetry (TG and DSC) of Mg2.5Al-LDH and RMg2.5Al&coumarin LDH powders

Thermal analysis (Thermogravimetric - TG) and calorimetric (Differential Scanning Calorimetry - DSC) were used to determine the thermal stability and powder degradation processes of: 1) LDH containing hydrotalcite with chemical formula $Mg_{2,5}Al(OH)_7(CO_3)_{0,5}(H_2O)_{2,5}$ - abbreviated Mg2.5Al-LDH (CHT2,5) and 2) LDH with coumarin organic chromophore embedded between the layers.

Intercalation of coumarin 343 (C343) into the hydrotalcite of $Mg_{2,5}Al(OH)_7(CO_3)_{0,5}(H_2O)_{2,5}$ (CHT2.5) by reconstruction leads to a composite material, herein after referred to as RMg2.5Al&coumarin. Figure 4.10 b shows thermogravimetric (TG) analysis and differential scanning calorimetry (DSC) of RMg2.5Al&coumarin. Generally, the curve shape is close to that for Mg2.5A1 in Figure 4.10 a.

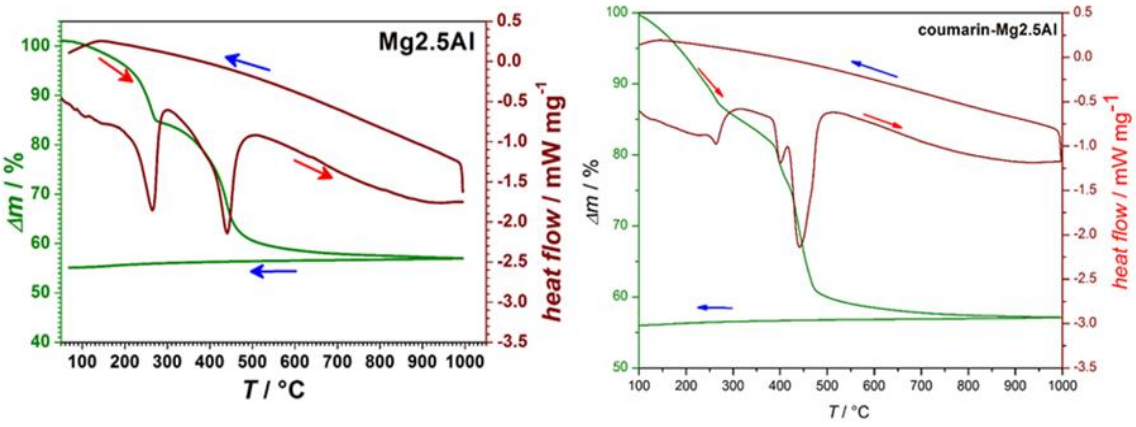

Figure 4.10 TGA and DSC diagrams of the Mg2.5Al-LDH and RMg2.5Al&coumarin LDH powders

4.4.3 Analyze FT-IR

4.4.3.1 Analyze FT-IR powders of Mg2.5Al, PMg2.5Al-DS and RMg2.5Al-DS

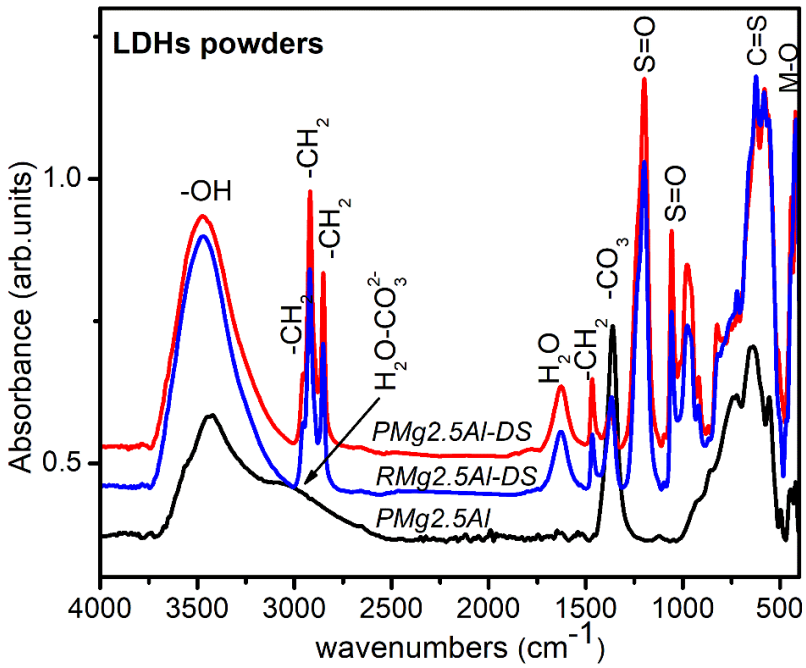

Figure 4.11 FTIR spectra of PMg2.5Al LDH and DS modified Mg2.5Al LDH powders

For all powders supposed to FTIR investigations, the broad absorption band in the 3500-3700 cm^{-1} region is determined by the stretching vibrations of the hydroxyl group involved in the interactions between the lamellar structures.

The DS interlayer intercalation is supported in the FT-IR spectra of PMg2.5Al-DS and RMg2.5Al-DS by the appearance of bands assigned to DS counterions at 2918 and 2852 cm^{-1}

corresponding to the CH_2 stretching vibrations, along with bending vibration at 1480 cm^{-1}[39, 40].

The characteristics SO_4 symmetric vibrations could also be evidenced in the 1197-1059 cm^{-1} band [43]. The CO_3^{2-} asymmetric stretching mode, around 1360 cm^{-1} characteristic to the interlayer carbonates visible in PMg2.5Al spectrum is still observable in the DS modified Mg2.5Al LDH powders as a result of atmospheric contamination.

4.4.3.2 FT-IR analysis of RMg2.5Al, RMg2.5Al&coumarin powder and of thin films deposited from RMg2.5Al&coumarin target

The spectra are typical for a LDH structure with a broad adsorption band at around 3500 cm^{-1} due to O-H stretching of both hydroxide layers and interlayer water molecules. The band is the most visible as expected in the reconstructed RMg2.5Al-LDH.

Furthermore, for this sample vibrations modes related to water are visible: a shoulder around 3000-3100 cm^{-1} caused by the interaction between CO_3^{2-} and H_2O present in the gallery and H_2O bending vibration around 1600 cm^{-1}.

The bands characteristics to metal-oxygen in the brucite layer appearing below 700 cm-1 are not so well defined in the above spectra.

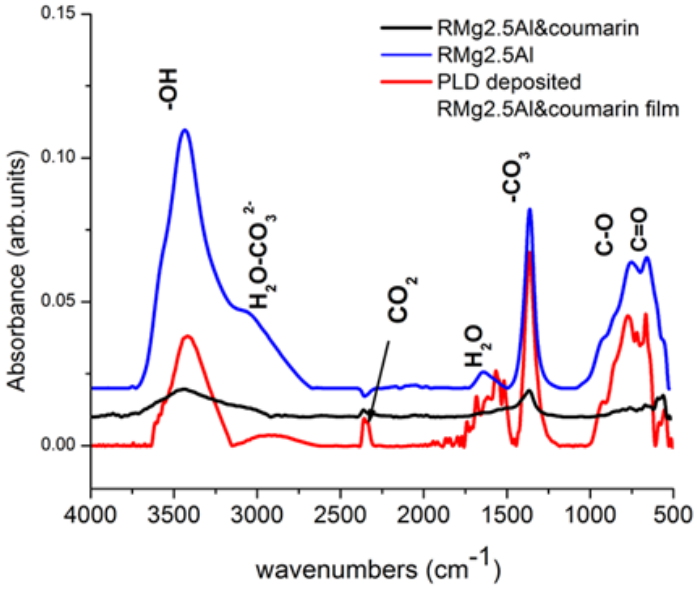

Figure 4.12 FTIR spectra of RMg2.5Al, RMg2.5Al&coumarin LDH powders and RMg2.5Al&coumarin thin films

The co-intercalation of CO_3^{2-} anions along with coumarin molecule prevents the aggregation of dye molecules and maintains the size effect in PL behavior.

4.5 Characterization of thin films obtained by PLD

4.5.1 XRD Characterization

4.5.1.1 XRD characterization of pristine Mg 2.5 Al-LDH thin films obtained by PLD

Laser working at two laser harmonics (266, 532) and fundamental (1064 nm) was used to ablate the pristine PMg2.5Al target. Less organized structures are formed following ablation at 266 nm laser wavelength. The c-parameters values included in Fig.4.13 are slightly larger compare to its corresponding PMg2.5Al target.

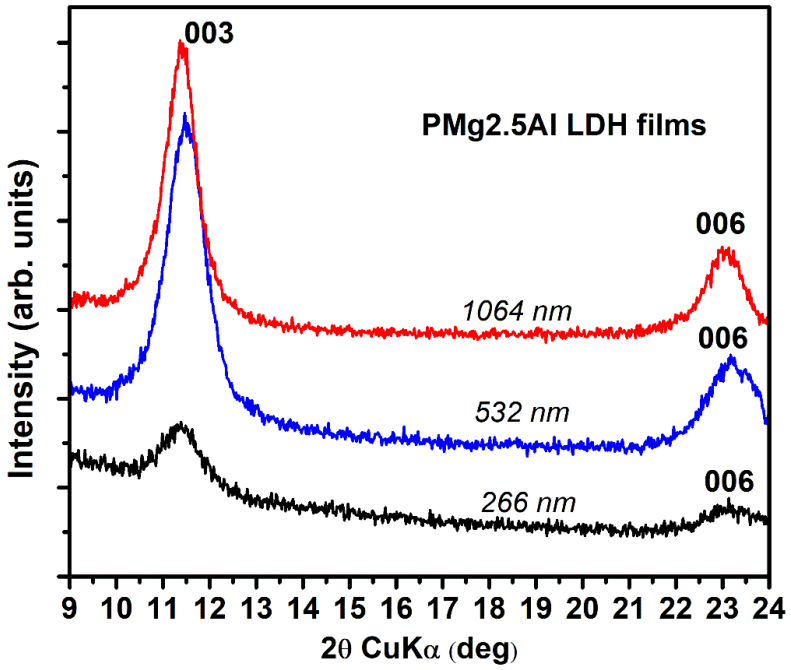

Figure 4.13 Representative XRD patterns of LDH thin films grown by PLD at 266, 532 and 1064 nm wavelengths

4.5.1.2 XRD characterization of PMg 2.5 Al-DS and RMg 2.5 Al-DS obtained by PLD

The XRD patterns of the thin films deposited from the DS-modified Mg2.5Al targets exhibit quite less defined peaks or their absence, stating for the formation of less oriented structures and the partial delamination of the LDHs (Fig.4.14). Only the (006) peak could be discriminated in the XRD patterns. The (003) peak is hindered by the large absorption at low angle. The deposition at 532 nm apparently favored the formation of organized layered structure. The result is endorsed by the thermal analysis proving a high thermal stability of the PMg2.5Al powder in comparison with the PMg2.5Al-DS and RMg2.5Al-DS ones.

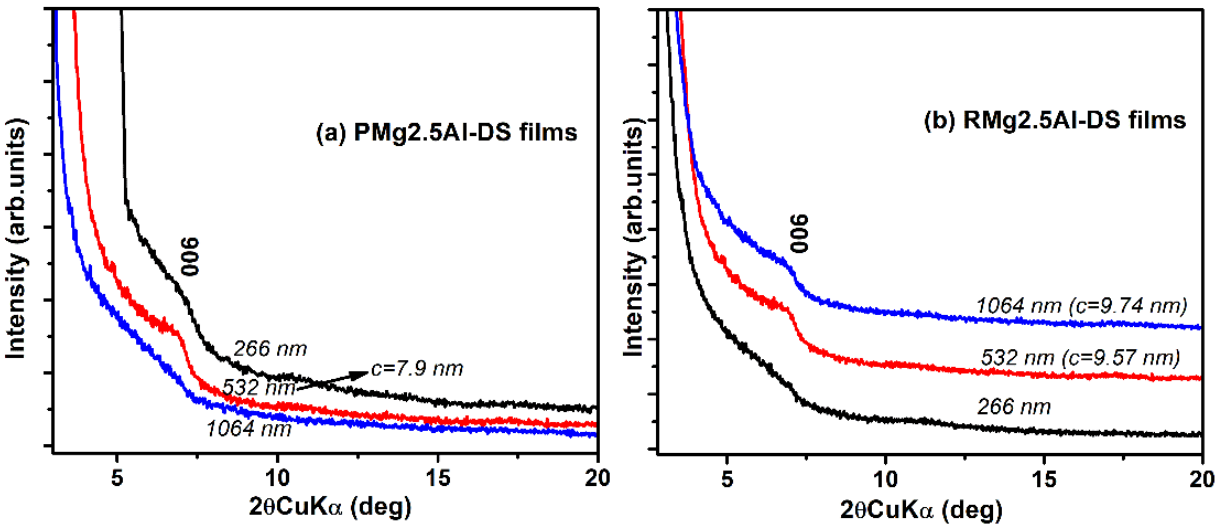

Figure 4.14 Representative XRD patterns of the (a) PMg2.5Al-DS films and (b) PMg2.5Al-DS films

4.5.1.3 XRD characterization of R-coumarin-Mg2.5Al-LDH

Thin films of Mg2.5Al-LDH and R-coumarin-Mg2.5Al-LDH were analyzed by X-ray diffraction (Fig 4.15, 4.16). In the deposition process, an essential role is played by the absorption of coumarin in the UV with the maximum specific at λ = 440 nm, because this property can well explain the high crystallinity of the R-coumarin-Mg2.5Al-LDH films and large coherent length (D003 = 12 nm) for films deposited at 532 nm wavelength compared to thin film at 1064 nm, even if the deposition conditions (fluence and number of pulses) were the same.

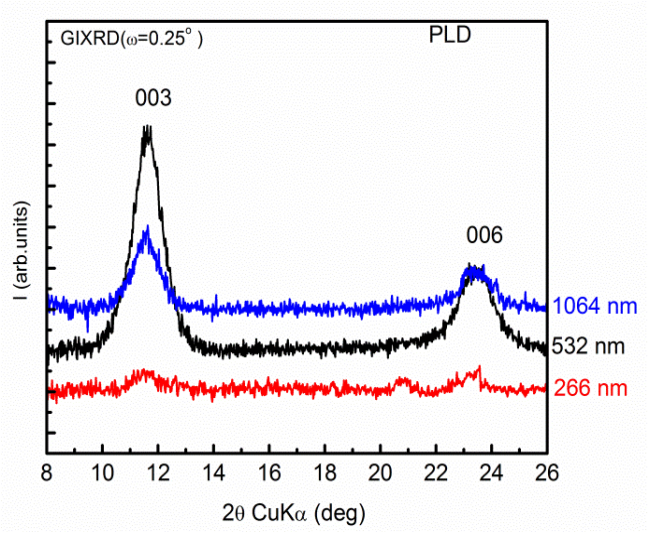

Figure 4.15 XRD patterns of the thin films deposited from the PMg 2.5 Al-LDH obtained using PLD at 266 nm, 532 nm and 1064 nm wavelengths

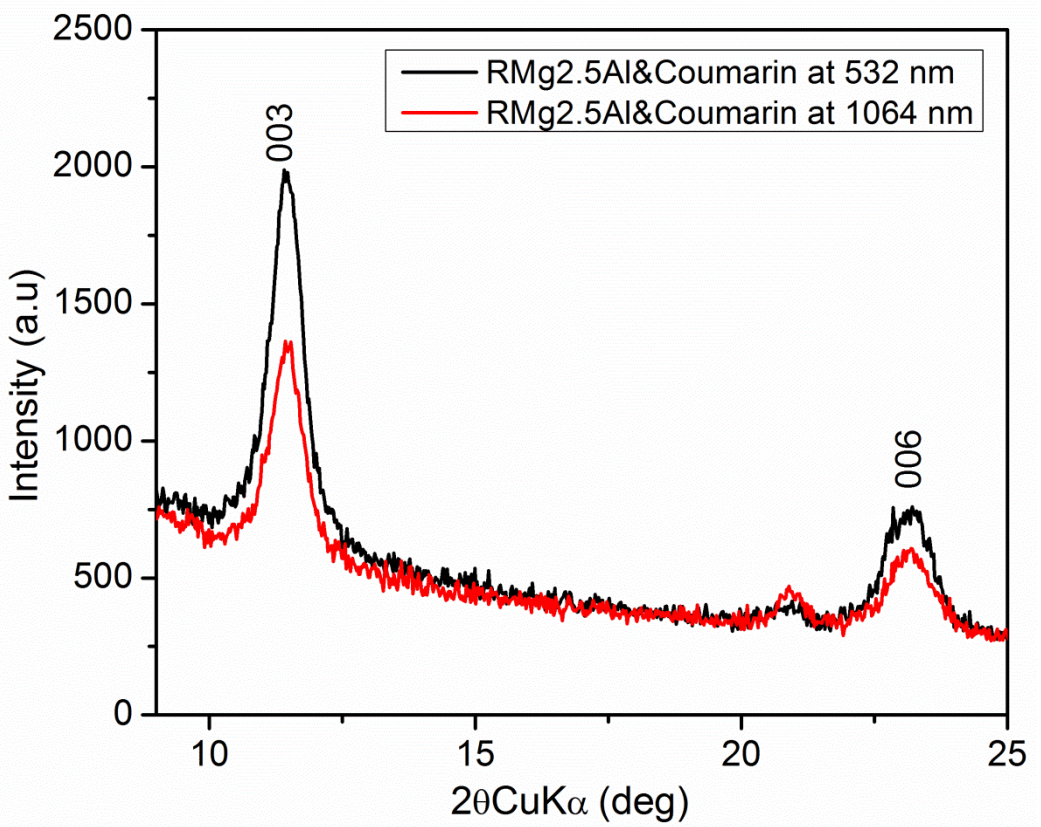

Figure 4.16 XRD patterns of the thin films deposited from the Coumarin-modified Mg2.5Al targets

The c-parameters values and the size of the crystallites calculated from the X-ray Diffractogram are shown in Table 4.6

Thin films	Deposition parameters	c(Å)	D_{003} (nm)
Mg2.5Al-LDH	532 nm	23.119	8
	1064 nm	23.369	9.5
Coumarin-Mg2.5Al-LDH	532 nm	23.177	12
	1064 nm	23.154	10

Table 4.6 The calculated lattice parameters obtained from XRD patterns of Mg2.5Al-LDH&Coumarine and Mg2.5Al-LDH thin films

4.5.2 FT-IR analysis

4.5.2.1 FT-IR analysis of PMg 2.5 Al-DS and RMg 2.5 Al-DS thin films obtained by PLD

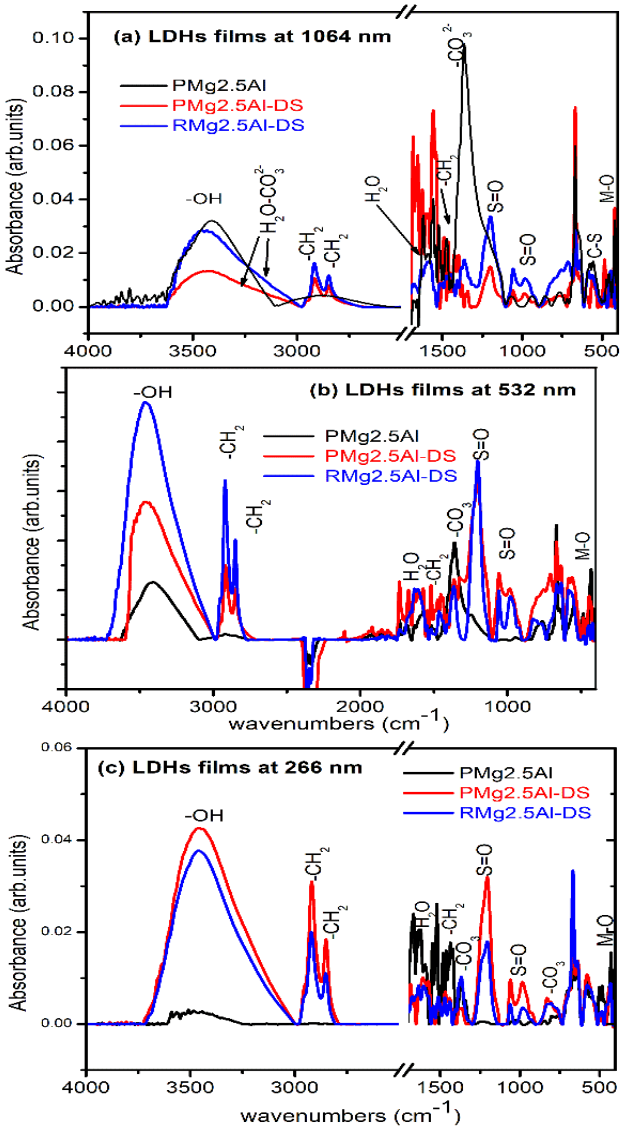

Figure 4.17 FTIR spectra of the PMg2.5Al-LDH, PMg2.5Al-LDH-DS şi RMg2.5Al-LDH thin films deposited by PLD at different wavelengths: 1064 nm (Fig a), 532 nm (Fig b) and 266 nm (Fig c)

FT-IR spectra of all the thin films deposited at the mentioned wavelengths presented in Fig. 4.17 show that the transferred films have the same structure as their respective LDH target. Stretching vibrations of S=O characteristic for DS, are clearly visible in all the thin films irrespective to the wavelength used for their deposition.

Associated with the presence of the broad OH^- band in all thin films FT-IR spectra, these stands for the deposition of the DS-modified LDH with the conservation of the organic interlayer anion. Some particularities could be extracted from the FT-IR spectra which are in agreement with the XRD results: high intensity of the interlayer CO_3^{2-} asymmetric stretching mode at 1375 cm^{-1} and of the water OH^- stretching vibration of the metal hydroxide layer and interlayer water molecule around 3500 cm^{-1} for the PMg2.5Al film

Apparently, the FT-IR spectra of the thin films deposited at 532 nm are the closest to the FT-IR spectra of their respective targets-powders.

4.6 Conclusions of Chapter 4

This chapter is structured in several parts that highlight both the stages of obtaining powders and deposition as thin films from solid targets with Pulsed Laser Deposition, as well as their morphological and structural analysis.

For the synthesis of the MgxAl (x = 2.5) Layer Double Hydroxide type used as reference samples, the co-precipitation method at low supersaturation and pH 10 was chosen. For the intercalation of Dodecyl Sulfate (DS) anion among lamellar layers of Layered Double Hydroxides, the co-precipitation and reconstruction at room temperature were selected as synthesis methods.

The next step was to obtain the solid targets used in thin film deposition experiments. In order to preserve the lamellar structure and the functionality of the intercalated molecules in their structure, the application of a thermal treatment was avoided, the hydrotalcite targets being obtained by mechanical pressing at 3-4 atm.

Thin films were deposited by PLD using three different wavelengths (1064 nm, 532 nm and 266 nm) and subsequently subjected to physico-chemical and morphological analyzes.

The X-Ray Diffraction confirmed the intercalation of Dodecyl Sulfate into the structure of hydrotalcite powders. Also, with this method, the successful transfer of unmodified hydroxides as well as hybrid hydroxides characterized by the preservation of "guest" molecules in the form of thin films was confirmed.

Fourier-Transform Infrared Spectroscopy (FTIR) analysis shows the specific structural characteristics of MgxAl (x=2.5) hydrotalcites and, furthermore, has the characteristics determined by total or partial intercalation of the guest molecule. This method confirmed the

intercalation of organic molecules but also their preservation after deposition of thin films. Optical investigations and analysis of post-measurement data confirm the results obtained with FTIR and XRD.

The images obtained by SEM and AFM of thin film surfaces deposited at the three wavelengths exhibit specific features of lamellar structures, but also disordered structures dominated by conglomerates and characterized by high roughness, determined by the organic and chromophore components in their structure.

In summary, the fabrication of pristine Mg2.5Al thin film and dodecyl sulfate intercalated between layers of Mg2.5Al by pulsed laser deposition technique on silicon substrates was performed. Based on the results provided from XRD, FT-IR and thermogravimetric investigation techniques successful intercalation of dodecyl sulfate into galleries of LDHs was demonstrated. Complex Mg2.5Al LDHs or DS-modified Mg2.5Al thin films structure were successfully obtained.

The pulsed laser deposition technique proves to be a suitable technique for deposition of such complex structures. The role of the three selected wavelengths 266, 532 and 1064 nm of Nd: YAG laser for the transfer of pristine Mg2.5Al LDH and intercalated DS in Mg2.5Al LDHs with the conservation of the organic anion in the interlayer space was observed from FT-IR and XRD patterns.

The PLD deposition at 532 nm secured better the transfer of the structural properties of the Mg, Al-LDH and DS functionalized Mg, Al -LDHs thin films. Therefore, this work provides a facile laboratory deposition method for fabrication of LDH thin films and organo-modified LDH thin films for the purpose of prospective application in corrosion protection coatings with oriented structure.

In conclusion, we have shown that the structural properties of coumarin dye within the Mg-Al layered double hydroxide thin films deposited by PLD are preserved.

Powder X-ray diffraction and FT-IR spectroscopy data demonstrated intercalation of coumarin in LDHs with a content of Mg/Al of 2.5.

The use of 532 nm wavelength laser for PLD deposition leads to the conservation of the organic anion in the interlayer space.

Inorganic system provide good support for chromophore dyes and opens great routes for fabricating functional luminescent materials by laser methods.

4.7 References to Chapter 4

[1] U.Costantino,V.Ambrogi,M.Nocchetti,L.Perioli **Hydrotalcite-like compounds: Versatile layered hosts of molecular anions with biological activity** , MICROPOROUS AND MESOPOROUS MATERIALS 107 (2008) 149-160

[2] D.Bäuerle Springer Verlag, ISBN 3540668918, (2000). **Laser Processing and Chemistry**

[3] Y.Kuang,L.Zhao,S.Zhang,F.Zhang,M.Dong and S.Xu **Morphologies, preparations and applications of layered double hydroxide Micro-/Nanostructures ,** Mater. 3 (2010) 5220-5235

[4] A.Vaccari **Clays and catalysis: a promising future** , Applied Clay Sci., 14 (1999) 161-198

[5] C.Mousty,F.Leroux **LDHs as Electrode Materials for Electrochemical Detection and Energy Storage: Supercapacitor, Battery and (Bio)-Sensor** , Recent Patents on Nanotechnology 6 (2012) 174-192

[6] Z.An,S.Lu,L.Zhao,J.He **Layered-metal-hydroxide nanosheet arrays with controlled nanostructures to assist direct electronic communication at biointerfaces** , Langmuir 27 (2011) 12745-12750

[7] J.M.Oh,D.H.Park,S.J.Choi,J.H.Choy **LDH Nanocontainers as Bio-Reservoirs and Drug Delivery Carriers Recent Patents on Nanotechnology** , 6 (2012) 200-217

[15] V.K.Sharma,P.D.Saharo,N.Sharmo,R.C.Rastogi **Excited state characteristics of acridine dyes: acriflavine and acridine orange** Spectrochim Acta A 59 (2003) 1161-1170

[16] S.Sardari,Y.Mori,K.Horito,R.G.Micetich,S.Nishibe,M. Daneshtakab **Synthesis and antifungal activity of coumarins and angular furanocoumarins** Bioorg. Med. Chem. 7 (1999) 1933-1940

[17] M.B.Maria,Z.Y.Wang **A dual-mode molecular switch based on a chiral binaphthol-coumarin compound** Tetrahedron Lett. 41 (2000) 4025-4028

[24] A.Matei,R.Birjega,A.Nedelcea,A.Vlad,D.Colceag,M.D.Ionita,C.Luculescu,M. Dinescu,R.Zavoainu,O.D.Pavel **Mg–Al layered double hydroxides (LDHs) and their derived mixed oxides grown by laser techniques** Appl. Surf. Sci., 257 (2011) 5308-5311

[25] A.Matei,R.Birjega,A.Vlad,M.Filipescu,A.Nedelcea,C.Luculescu,R.Zavoainu,O.D. Pavel,M.Dinescu **Adsorption properties of Mg–Al layered double hydroxides thin films grown by laser based techniques** Appl. Surf. Sci., 258 (2012) 9466-9470

[26] A.Vlad,R.Birjega,A.Matei,C.Luculescu,B.Mitu,M.Dinescu,R.Zavoainu,O.D.Pavel **Retention of heavy metals on layered double hydroxides thin films deposited by pulsed laser deposition** Appl. Surf. Sci., 302 (2014) 99-104

[35] M.Wei,Q.Yuan,D.G.Evans,Z.Q.Wang,X.Duan **Layered solids as a "molecular container" for pharmaceutical agents: L-tyrosine-intercalated layered double hydroxides** J. Mater. Chem. 15 (2005) 1197-1203

[36] B.Du,Z.Guo, Z.Fang **Effects of organo-clay and sodium dodecyl sulfonate intercalated layered double hydroxide on thermal and flame behaviour of intumescent flame retarded polypropylene** Polymer Degradation and Stability 94 (2009) 1979–1985

[39] M.Mora,M.I.Lopez,C.Jimenez-Sanchidrian,J.R.Ruiz **MIR and NIR spectroscopy of sol–gel hydrotalcites with various trivalent cations** Journal of sol-gel science and technology, 55, (2010), 59–65

[40] S.Velu,V.Ramkumar,A.Narayanan,C.S.Swamy **Effect of interlayer anions on the physicochemical properties of zinc–aluminium hydrotalcite-like compounds** Journal of Material Science, 32 (1997) 957–964

[43] C.Yilmazet, U.Unal, H.Y.Acar **Platelets to rings: Influence of sodium dodecyl sulfate on Zn–Al layered double hydroxide morphology** J. Solid State Chem. 187 (2012) 295-299

[45] S.Miyata **The Syntheses of Hydrotalcite- Like Compounds and Their Structures and Physico-Chemical Properties I: The Systems Mg2+-Al3+-NO3−, Mg2+-Al3+-Cl−, Mg2+-Al3+-ClO4−, Ni2+-Al3+-Cl− and Zn2+-Al3+- Cl−.** Clays Clay Miner 23 (1975) 369-375

[47] D.G.Evans,D.A.Xue **Preparation of layered double hydroxides and their applications as additives in polymers, as precursors to magnetic materials and in biology and medicine** Chem. Commun., (2006) 485-496

CHAPTER 5

General conclusions and further work

The last chapter of the doctoral thesis presents a summary of the main results obtained and reported in this study, reported to the initial objectives.

The first two chapters describe the fundaments of the study topics and an introduction to the issues approached in this thesis. Experimental and theoretical aspects of thin film laser-based deposition techniques have been explained, and investigative methods have been described for understanding and describing phenomena involved during experimental processing.

The main results presented in this paper and the original contributions can be synthesized as follows:

In Chapter 3, a large class of solvents was investigated to obtain hybrid polymerically films containing antitumoral agent in their composition, interconnection of physicochemical and biological results confirming the ability of MAPLE technique to obtain thin films of soft polymeric materials.

The deposition of PEG-PVA and PEG-PVA + curcumin thin films was performed by Matrix Assisted Pulsed Laser Evaporation on Si (001) and glass substrates. For these depositions, the Nd: YAG laser system was used at the 266 nm wavelength and a 10 Hz frequency and the laser fluence of 0.4 J / cm^2.

The concentration of copolymer and curcumin was kept constant at 3% wt. throughout all experiments, but several types of solvents were used: Chloroform, DMSO, H_20, H_2O+EtOH and Benzene.

The obtained films were analyzed by Spectro-Ellipsometry and AFM to determine thickness and roughness and to study stability in aqueous media. A strong influence of the solvents on film thickness and roughness was observed.

Atomic Force Microscopy (AFM) studies reveal the influence of solvents in MAPLE depositions; uniformly coated films are obtained in the case of Chloroform, DMSO and Benzene,

in contrast to water-based films and ethanol-water combinations characterized by unequally coatings in thickness and conglomerates spread randomly.

Fourier Transform Infrared Spectroscopy (FTIR) confirms the preservation of the polymeric structure and biological agent after transfer to substrates, the physicochemical properties and thin film functionality being also maintained.

We have demonstrated by Spectro-Ellipsometry and UV-Vis Spectro-Photometry studies the dependence of anti-tumoral agent release on the degree of degradability of thin films. Correlation of the results demonstrates that films characterized by rapid degradation also exhibit a sudden drug release, (thin films of PEG-PVA+curcumin$_{DMSO}$).

We have tested the anticancer properties by biologically evaluating PEG-PVA + curcumin films in terms of viability and cell proliferation of osteosarcoma cells MG-63. The results demonstrate the cytotoxic and antiproliferative potential as well as conditioning the results of the degree of degradation and the proportion of drug released in well-established time intervals. The most active thin film is PEG-PVA+curcumin$_{DMSO}$.

The above results revealed the anti-cancer character of thin PEG-PVA and PEG-PVA + curcumin films obtained by Matrix-Assisted Pulsed Laser Evaporation.

Chapter 4 highlights the potential of PLD technique in deposition of hybrid thin films of Layered Double Hydroxides which have incorporated into their structure organic molecules and photo-functional chromophores. Also, here are presented structural properties (FTIR and X-Ray Diffraction), morphological (AFM and SEM studies), but also the optical characteristics (UV-VIS spectroscopy studies) of powders and films.

The synthesis of MgxAl (x = 2.5) Layer Double Hydroxide powders used as reference samples was performed. The co-precipitation method at low supersaturation and pH 10 was chosen for their preparation. Intercalation of Dodecyl Sulfate (DS) anion between the LDH layers was accomplished by two synthesis methods: co-precipitation and reconstruction in aqueous solution at room temperature. For the preparation of nanocomposite hydrotalcite powders functionalized with the "guest" molecule of the class of organic chromophores, reconstruction in aqueous solutions at room temperature was used.

The solid targets obtained from the powders synthesized in the first stage of the study were obtained, these being made by mechanical pressing to avoid damaging of the lamellar structure and the functionality resulting from the application of a thermal treatment.

The deposition of thin films of Layered Double Hydroxides (LDH) containing organic anion of Dodecyl Sulphate and coumarin was performed by Pulsed Laser Deposition on Si (001) and Quartz substrates. For these depositions, the Nd: YAG laser system was used at three different wavelengths (1064 nm, 532 nm and 266 nm) at a frequency of 10 Hz and laser fluence of 2 J/cm^2.

The intercalation of organic molecules in powders has been confirmed, along with the preservation of their properties after thin film deposition. These has been proven by Fourier Transform Infrared Spectroscopy (FTIR) and X-ray Diffraction (XRD) investigations. Characteristics specific to hydrotalcites as well as those determined by the intercalation of "guest" molecules are highlighted by these methods. In conclusion, it can be said that the main objectives imposed at the beginning of this study were achieved, among which:

a) Finding and optimization of experimental parameters suitable for the laser-based depositions;

b) Successful employment of Pulse Laser Deposition (PLD) for the production of high quality thin films of Layer Double Hydroxides (LDH) and LDH with organic molecules and chromophores embedded used for various applications;

c) Physico-chemical characterization in order to understand the complex phenomena that occur during the deposition;

d) Successful employment of the matrix-assisted pulsed laser evaporation (MAPLE) for the fabrication of polymeric hybrid coatings;

e) The study of physico-chemical properties and in vitro testing of MAPLE films for medical applications;

The results of this study, together with several issues that were not approached during this work, have opened a number of possible subjects for future research;

Investigation of other experimental parameters such as the modification in the number of pulses and the concentration of polymeric and biological materials in order to obtain and functionalization the PEG-PVA thin films with embedded curcumin;

Investigation of antibacterial properties of polymeric hybrid coatings;

Use of Pulsed Laser Deposition (PLD) technique directly for the deposition of LDH films from complexes targets containing both DS and chromophoric compounds;

CURRICULUM VITAE

Published and disseminated results

Articles published by the author in ISI ranked journals:

I.Tirca, V.Mitran, V.Marascu, S.Brajnicov, V.Ion, F.StokkerCheregi, I.A.Popovici, A.Cimpean, V.Dinca, M.Dinescu, ***In vitro*** **testing of curcumin based composites coatings as antitumoral systems against osteosarcoma cells** Appl Surf Sci, 425 (2017) 23-30

A.Vlad, R.Birjega, I.Tirca, A.Matei, C.C.Mardare, A.W.Hassel, A.Nedelcea, M.Dinescu, R. Zavoianu **Pulsed laser deposition of functionalized Mg–Al layered double hydroxide thin films** APPL PHYS A-MATER, (2018) 24:152

Regular works presented by the author at international conferences:

1. Tirca I.; Dumitrescu N. L. ; Marascu V. ;Bonciu A. ;Brajnicov S. ; Dinescu M. ; Dinca V. ; " Fabrication and characterization of Poly(vinyl alcohol)/Poly(ethylene glycol) thin films for biological applications" ; The 8th international conference on advances materials , 7-10 , iulie , 2015, Bucuresti , Romania ; 946;

2. Dumitrescu N.L. ; Tirca I. ;Bonciu A. ;Marascu V. ;Brajnicov S. ;Dinescu M. ;Dinca V. ; "Study of the solvents influence on the morphological and chemical characteristics of hydroxyapatite thin films deposited by MAPLE";The 8th international conference on advances materials, 7-10, iulie, 2015, Bucuresti, Romania;942

3. Tirca I. ;Palla Papavlu A. ; Filipescu M. ; Dinca V. ; Dinescu M. ; Cremer L. ; Calugaru A. ; Vlase E. ; Coman C. ; "Captopril drug delivery sistems via matrix-assisted pulsed laser evaporation";E-MRS 2015 Spring Meeting;11-15;mai;2015;Lille; France;CC 28;

4. S. Brajnicov ; L. Rusen ;M. Filipescu ; N. L. Dumitrescu ; I. Tirca ; M. Dinescu ;V. Dinca ; "Atomic force microscopy study of Polyethyene glycol Polycaprolactone methyl ether copolymer coatings obtained by Matrix Assisted Pulsed Laser Evaporation ";The 8th international conference on advances materials, 7-10, iulie, 2015, Bucuresti, Romania;935

5. A. F. Bonciu ; C. R. Luculescu ; I. Tirca ; "MAPLE gradient deposition of hydroxyapatite-based biocompatible films for tissue engineering" ; The 8th international conference on advances materials, 7-10, iulie, 2015, Bucuresti, Romania;1000

6. I. Tirca , A. Palla Papavlu , L. Cremer , A. Călugaru , E. Vlase , C. Coman , M. Dinescu ;

"Application of laser-based methods for the fabrication of Captopril transdermal patches" Conferinta anuala de Imunologie 2-4 , octombrie , 2015 , Bucuresti , Romania

7. I. Tirca , V. Marascu , V. Ion , S. Brajnicov , V. Dinca and M. Dinescu " Hybrid biodegradable copolymer based coatings for in vitro osteosarcoma studies " ; E-MRS 2016 Spring Meeting ; 2-6 mai 2016 Lille France ;

8. A. Vlad , R. Birjega , A. Matei , I. Tirca , M. Dinescu , R. Zavoianu , O.D. Pavel , M.C. Corobea; "Nanocomposite dodecylsulfate-modified Mg-Al layered double hydroxide thin films deposited via laser technique" NANOTECH 2016 ; 22-25 , mai , 2016 , Washington , DC

9. I. Tirca , V. Marascu , S. Brajnicov , V. Dinca , D. Pelinescu , I. Sarbu , V. Mitran , A. Campean , M. Dinescu "In vitro evaluation of antitumoral activities of Curcumin loaded biodegradable copolymer" ,Bucharest University Faculty of Physics 2016 Meeting , 17 iunie 2016 ,Bucuresti , Romania

10. I. Tirca , V. Marascu , N. L. Dumitrescu , A. Bonciu , S. Brajnicov , V. Ion , M. Dinescu , V. Dinca "Curcumin loaded biodegradable copolymer coatings obtained by MAPLE technique" , Bucharest University Faculty of Physics 2015 Meeting , 19 iunie 2015,Bucuresti,Romania

11.L.N. Dumitrescu, I. Tirca, V. Ion, A. Moldovan, V. Marascu, V. Dinca, M. Dinescu "Polyvinylideneflouride thin films deposited by MAPLE" ICPEPA-10 10TH INTERNATIONAL CONFERENCE ON PHOTOEXCITED PROCESSES AND APPLICATIONS, AUGUST 29 – SEPTEMBER 2 , 2016, Brasov , Romania

12. A. Marinescu , A. Matei , A. Vlad , R. Birjega , M. Filipescu , V. Marascu , M. Dinescu , I. Tirca , R. Zavoianu ,O. D. Pavel , C. Corobea "The selection of optimal deposition conditions for producing thin films of Mg-Al LDH using laser techniques" ICPEPA-10 10TH

INTERNATIONAL CONFERENCE ON PHOTOEXCITED PROCESSES AND APPLICATIONS, AUGUST 29 – SEPTEMBER 2 , 2016, Brasov , Romania

13. I. Tirca , V.Marascu , S.Brajnicov , V.Dinca , D. Pelinescu , I. Sarbu , V. Mitran , A.Campean , M.Dinescu "In vitro evaluation of antitumoral and antibacterial activities of Curcumin loaded biodegradable copolymer" ICPEPA-10 10TH INTERNATIONAL CONFERENCE ON PHOTOEXCITED PROCESSES AND APPLICATIONS, AUGUST 29 – SEPTEMBER 2 , 2016, Brasov , Romania

14. A. Vlad , I. Tirca , R. Birjega , A. Matei , M.Dumitru , M. Dinescu , V. Marascu , R. Zavoianu , M. C. Corobea "Comparison of different routes for the manufacture of intercalated dodecyl sulfate Mg,Al-layered double hydroxides composite thin films using laser techniques" ICPEPA-10 10TH INTERNATIONAL CONFERENCE ON PHOTOEXCITED PROCESSES AND APPLICATIONS, AUGUST 29 – SEPTEMBER 2 , 2016, Brasov , Romania

15. A. Vlad , R. Birjega , A. Matei , I. Tirca , M. Dinescu , R. Zavoianu , M.C. Corobea "Conditions for the deposition of organo-layered double hydroxides hybrid thin films by laser techniques" 3ICPAM-11 11th International Conference on Physics of Advanced Materials September 8-14, 2016, Cluj-Napoca, Romania

16. A. Vlad , R. Birjega , A. Matei , I. Tirca , R. Zavoianu , O.D.Pavel , M.C.Corobea , M. Dinescu "Hybrid organic chromophores-layered double hydroxide thin films deposited via laser techniques"

E-MRS Fall 2016 September 19 -22, 2016, Warsaw, Polonia

17. L.N. Dumitrescu , I. Tirca , A. Bonciu , V. Marascu ,V. Dinca , M. Dinescu "Morphological and topographical investigation of PVDF thin films deposited by matrix assisted by pulsed laser evaporation" THE 5th INTERNATIONAL COLLOQUIUM "PHYSICS OF MATERIALS" (PM 5) 10-11 Noiembrie 2016 , Bucuresti , Romania

18. I. Tirca, A. Vlad, A. Rotaru, R. Birjega, M. Secu, A. Matei, R. Zavoianu ,M.Dinescu "Coumarin intercalated layered double hydroxides thin films prepared by laser techniques" Central and Eastern European Committee for Thermal Analysis and Calorimetry. 28-31 august 2017, Chisinau, Moldova

19. I. Tirca, A. Vlad, M. Secu, R. Birjega, R. Zavoianu, V. Marascu, A. Marinescu, M. Dinescu

"Properties of Layered Double Hydroxides (LDHs) thin films deposited by laser techniques" Central and Eastern European Committee for Thermal Analysis and Calorimetry. 28-31 august 2017, Chisinau, Moldova

20.A.Vlad,R.Birjega,I.Tirca,A.Matei,A.Rotaru,R.Zavoianu,C.C.Mardare,A.W.Hassel,M.Dinescu "The fabrication of organic-inorganic thin films based on layered double hydroxides materials using laser techniques" E-MRS 2017 Spring Meeting ; 22-26 mai 2017 Strasbourg, Franța ;